SECOND SERIES VOL. VII, No. 8.

BULLETIN

OF

THE NEW YORK ACADEMY OF MEDICINE

AUGUST, 1931

INCORPORATED 1851

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EDITORIAL

AN EPITOME OF THE HISTORY OF SPANISH MEDICINE.[1]

The status of Spanish medicine, as of Spain itself, in relation to Europe, turns upon the physical geography of the country, its peculiar isolation by sea and Pyrenean mountain-walls, and the isolation of its different provinces from one another by physical barriers of the same kind. Apart from the work of the great histologist Ramón y Cajal, Spain has left no appreciable mark upon European medicine, no such influence (shall we say) as that of Spanish fiction upon the French and English novel of the 17th-18th Centuries, of Calderon upon Shelley, of Velázquez upon Whistler or of Goya upon the whole range of recent fantastic and realistic art. Yet, during her Golden Age (1516-1700), Spain was one of the greatest colonizers the world has known, in Velázquez she produced the greatest painter who ever lived, and, as we shall see, her output in medicine during 1500-1700 holds its own with any other European country except Italy in the 16th Century and England in the 17th. Taken by and large, the medicine of Spain was, and still is, virtually the medicine of South America, Mexico, Central America, the Antilles, the Philippines, Portugal, Goa and parts of North Africa. In her power to assimilate native races to herself, Spain was a more efficient colonizer than Rome or England, actually getting inside their skins and making them Spanish at heart and in

[1]From the Institute of History of Medicine, Johns Hopkins University, Baltimore, Md. Direction of Professor William H. Welch.

modes of thought. Rome, England, Prussia could impose laws and uphold government, but Rome could not change the essential nature of the Gaul, the Teuton, the North African or the Jew; England could not make Englishmen out of Hindus or Australian aborigines, nor could Spain, in the days of her might, turn Neapolitans and Sicilians into Spaniards. Her influence upon native races was more pervasive and intangible, like that of the Greeks upon the peoples of Egypt or of the littoral of Asia Minor. When Blasco Ibañez asserted that Spain has no further need of colonies, since their peoples have all become her spiritual children, the assertion met with no particular comment, for all recognize it to be the truth.

The history of Spain and of Spanish medicine goes back to palæolithic times. The Iberian peninsula, surrounded by the Atlantic and the Mediterranean and shut off from France by the Pyrenees, was once continuous with Africa, and, as some enthusiasts conjecture, even with America. From the heights of Castile and Estremadura falls a slope which is abrupt toward the Mediterranean, gentle toward the Western ocean. These gradients are criss-crossed by smaller cordilleras and plateaus, separating Spain from Portugal, old Castile from New Castile, Castile and Estremadura from Andalusia, while Aragon, Catalonia, Valencia and part of La Mancha form the narrow littoral on the Mediterranean (Northern) coast. The valley of the Ebro lies in Aragon and Catalonia and between the Ebro and the Guadalquivir is a tableland of huge dimensions. Over this well ridged and well-rivered peninsula, there passed, in due process of time, the usual succession of domineering or dominating races—Iberians, Celts, Phœnicians, Visigoths, Romans, Moslems, with constant insurrection of groups of subjugated peoples, with natural coalition of adjacent kingdoms or the inevitable secession from such mergers, until finally the Moslem yoke is thrown off and Spain stands forth as an independent, individualized nation, through the union of Castile and Aragon under Ferdinand and Isabella in 1479. So England was formed out of the Saxon heptarchies, so modern France, Italy and

Russia were formed, so the Germany of 1870 was formed and so our own country was federalized and unified after 1865. In the view of Humboldt, the initial primitive Celt-Iberian stock was autochthonous, aboriginal, of the soil. In the view of Leibnitz, Niebuhr and Haeckel, they were a Hamitic-Semitic race of North African origin, *colorati vultus et torsi plerumque crines,* like the Sicilians in Tacitus. The longish skulls, the similarity in language and primitive tribal organization, point to a close relationship with the Berbers, Touaregs, Copts and Kabyles of the North African littoral and desert. The Spanish Basques west of the Pyrenees are dolichocephalic; the French Basques brachycephalic. The Touareg suffix *tani* is common to the Roman geographical designations Lusitania (Portugal), Gaditania (Cadiz), Mauritania and, as stated, the Iberian peninsula was once continuous with Africa Minor. The carvings, rude line engravings and mural paintings of this prehistoric Afro-Semitic race constitute the finest and most instructive survival known to us of palæolithic art. In the caverns of Cogul (Lerida), Alpera (Albacete) and Almeria are fresco paintings and etchings on stone or bone, which are so accurate and realistic that the animals are identifiable as to species and the human figures are perceived to be almost identical as to costume and physical habitus with those of Crete. As in the case of Egypt, this strong grip upon reality vanishes in the neolithic art of Spain, which is decadent and remarkable only in respect of decorative pattern work and ornamentation.[2] The primitive inhabitants, both of Spain and the Canary Islands, were indubitably of the Crô-Magnon type. There is no evidence of the existence of Neanderthal Man. The West and the Northwest (Galicia and Portugal) was settled by the Celts, the Iberians occupying Eastern and Southern Spain, while in the center the Celt-Iberian mix-

[2]The observation of anthropologists is to the effect that palæolithic art, like that of the savage, the child and the insane, is animistic, ideographic and realistic, while the inevitable tendency of neolithic art toward pattern work and formal, but lifeless perfection, is a natural consequence of development of the science of measurement, e. g. in the designs of pottery, textiles, architecture and other metric and geometric arts.

ture came to pass. The provinces, such as Lusitania or Galicia, were local federations of 30-40 tribal groups. The Phœnicians came into Spain in the 11th Century B. C., attracted by the mineral wealth (silver, copper, mercury). They called the peninsula *Span* or *Spania* (the hidden land). The Greeks came in on the northeastern coast (630 B. C.) and have left the earliest accounts of the country (6th Century B. C.). The Carthaginians came in on the eastern seaboard a century later. During 236-206 B. C., Spain was in the hands of the Barca *gens*. Hamilcar Barca gave his name to Barcelona, on the northeastern coast, while his son-in-law, Hasdrubal left another mark of Carthaginian occupation further south, in the name of the capital, Cartagena. In 206 B. C., the Carthaginians were ousted by the younger Scipio and the Romans occupied Spain during the next six centuries (206 B. C.-409 A. D.). They left their mark in better laws, better administration, in the remains of the great walls, public works, amphitheatres and aqueducts (Segovia, Tarragona), in the structure and etymology of the Spanish language,[3] in the well-made military roads, in the expansion of commerce, in long periods of peace which insured the growth of wealth and culture, and in the development of the best type of citizenship. Some of the mildest and greatest of the Roman emperors, Trajan, Hadrian,[4] Theodosius, were all of them born at Italica, near Seville, and Marcus Aurelius was of Spanish descent. Augustus Caesar, who put his Spanish freedman, Hyginus, in charge of the Palatine Library, was once at Tarragona, where he was cured of a liver complaint by Antonius Musa. To the Roman literature, Spain contributed Martial, Lucan, Quintilian, the Senecas, Columella, Pomponius Mela and Juvencus. Among the medical men, the anatomists Mustio and Vindician and the physicians Cassius Felix, Theodorus Priscianus and Caelius Aurelianus were Numidians or "little

[3]Thus Zaragoza derives from *Caesaria Augusta*, Merida from *Emerita Augusta*, Badajoz from *Pax Augusta*, Astorga from *Asturica Augusta*, León from *Urbs Septima Legionis*, etc.

[4]Author of the *Animula vagula blandula* verses.

Africans" (from Africa Minor). By the 3rd Century A. D., there were many Christian communities in Roman Spain. St. Damasus (304-384), thirty-sixth in the line of Roman pontiffs, who inspired St. Jerome to translate the Bible, was of Spanish origin. Prudentius and Orosius came from Tarragona, Priscillian from Cordova, Theodolphus, author of the Palm Sunday *Gloria,* was Spanish born, and several martyrs of the Church, such as San Vicente of Valencia, Santa Eulalia of Merida, San Severo of Barcelona, Santa Leocadia of Toledo and Santa Engracia of Zaragoza, were put to death under Diocletian. At the beginning of the 5th Century, A. D., the Vandals swarmed into Spain to occupy Andalusia (Vandalusia or Vandal-Land) and were followed by the Visigoths, who dominated the country for three centuries (409-713). The principal relic of their occupation is the Visigothic Code (*leges barbarorum*), which contains certain rigorous prescriptions touching medical fees, punishment for malpractice and the reciprocal rights of physician and patients, not unlike those in the Code Hamurabi. The Visigothic Code was later combined with certain juridical principles enunciated by Isidore of Seville, to form the Spanish Magna Charta (*Fuero Juzgo*). The Romans held on until the Visigothic King Theodoric made a definite split with the Western Empire in 476. Toledo became the Visigothic capital during the reign of Athanagild (554-567) and about 587-589, the Visigoths were converted to Catholic Christianity. In the 6th Century, a Cæsarean section was performed by Bishop Paul of Merida (530-560) and a hospital was founded in the same city by Bishop Masona in 580. The most important figure among the Spanish clergy was Archbishop **Isidore of Seville** (570-636), whose statue stands in front of the National Library at Madrid beside that of Alphonso the Wise, and whom Sudhoff defines as "the true stepping stone to Spanish science and medicine in the Middle Ages." Like Cassiodorus and Boethius, Isidore was a man of vast learning, author of an universal history, a history of the Visigoths, Vandals and Suevians, lives of illustrious men, and the *Etymologia,* or encyclopædia of origins and ety-

mologies, which sums up all the knowledge of antiquity. The fourth book is devoted to medicine and derivations of medical terms. To the *Fuero Juzgo* or Spanish Charter, (*Forum Judicium*), Isidore contributed the doctrines of the divine right and hereditary succession of kings and the duty of the State to protect the Church, as the best means of insuring peace and tranquility in these troublous times.

During the long period of Moslem domination (711-1276), there was constant warfare, but the intervals of peace were far more frequent than during the period of struggle for national unity (1276-1479) and in these intervals, Christian, Moslem and Jew managed to subsist side by side without any apparent friction, like the wild animals at railhead in Uganda. The unitarian, standardizing mania of Islam was, in theory, at least, a species of theological Sovietism, but the real object of the emirs was conquest as a pathway to pleasure, with monotheism as a stalking horse. The Arabs themselves were sceptical, materialistic, indifferent, pleasure-loving, polygamous, sometimes atheistic, fonder of music, dancing and erotic poetry than of orthodoxy and devotion. Like all converts to a creed or a social code, the Berbers and other North African tribesmen were inevitably more fanatical than those born and bred in the faith. Arab military expeditions were usually forays for plunder and once the booty was secured, religious toleration was the rule. Christians acclimated to Moslem rule (Mozarabs), Moslems living under Christianity (Mudéjares) and Jews were, in fact, better treated by Islam than were the converted Jews (Maranos) and converted Moslems (Moriscos) under Christianity in the later period. Christian and Moslem observed the same holy days, and, in one instance, worshipped in separate halves of the same church. The Jews, under stress of the Visigothic penal code, went over to the Arabs, and became prime movers in the intellectual predominance of Cordova and Toledo. Again, the Arabic community was always tribal (*taifa*), sometimes nomadic. Alliances and allegiances were impermanent, often fitful and irresponsible. The whim of joining up with one's enemies, to help

them out in a tight place or against some hated rival, was as common to Christian or Moslem chieftains as it is to "the indifferent children of the earth" today. Ruy Diaz, far from being the noble, impeccable Christian warrior of tradition, ever crusading against the Paynim, was actually banished from Castile by Alphonso VI for theft of funds, sold himself on occasion to any highest bidder, got his romantic title of Cid (Lord and Master) from his Moslem employers, and, in 1086, appeared with a mixed horde of Christians and Moslems to dispossess the Moslem overlord of Valencia. When Ferdinand II (San Fernando) of Castile was invited by Louis XI to join the Crusades, he replied: "There are plenty of Moors in my own country." Single-minded fanaticism was confined to the Almoravides (religious men) or Berber converts of the Sahara, and to their opponents, the Almohades or unitarian Moors of Morocco. Under the tolerant Arab sway, literature, art, science and philosophy were permitted to flourish, hospitals and libraries were built, schools and scientific societies were founded, agriculture and industry were organized, and by the 10th Century, when the nomads became sessile and stabilized, Moslem Spain, and its capital Cordova, were credited with untold wealth. Apart from the mathematics and polite literature, the Moslems were assimilators and transmitters rather than innovators. Their architecture (domes and decorated flat surfaces) derived from Byzantium. The *patio* or enclosed court of their houses came from Rome. Their medicine was but a diluted or debased strain of Greek medicine. The Moslems were, nevertheless, the principal transmitters of ancient Greek and Byzantine Greek culture. The handy Arabic numerals made arithmetic (algorythmics) possible, the Moslems forwarded algebra as well as the Egyptian tradition of chemistry (alchemy) and one of their great physicians, Avicenna, was the founder of geology. To the comforts and luxuries of life the Arabs added cultivated plants and drugs, spices and perfumes, gardens, street-lamps, window-panes, fireworks, under-garments, morning and evening serenades with stringed instruments. The

great physicians of the Western Caliphate (655-1236)—Albucasis, Avenzoar, Averroes and Moses Maimonides—were all born at (or near) Cordova, but they are regarded by the Spanish historians as part and parcel of Islam or Israel, not germane or essential to the development of Spanish medicine in the Age of Gold. Beyond a few, fugitive and fragmentary strains of Mozarabic melody, monotonous and fitful as the crooning of a negress at a clothes-line, the Moslems left no appreciable influence on the national music of Spain, which is *sui generis*. One of these Mozarabic chanties, *Qualbi qualb' Arabi qualb' Arabi* ("My heart is the heart of an Arab") suggests the fact that the nomad warriors of the desert did not, like the Visigoths, bring their families with them and so intermarried freely with the Christian women. The main area of this racial inmixture of Celtiberic, Visigothic and Afro-Semitic strains was Andalusia (at the South) and through the fact that the Spanish colonization of the Western Hemisphere was accomplished mainly by Andalusians, sailing from the convenient ports of Cadiz and Seville, the effect of this Arabic racial ply upon national character was to be most decisive among the peoples of the New World.

To the North of the Cordovan Caliphate, which, during 910-1037, embraced most of the Iberian peninsula, lay the Visigothic kingdoms of Asturias, Leon, Castile, Navarre and Catalonia (Barcelona) and of these, the mountainous border state of Asturias was the center of continual revolt from the Moslem yoke from the start. The frontier was South of the Douro River and Aragon was in the enemy domain. By 1150, this frontier has been pushed southward to the Tagus River and by 1276, all that remained of Moslem Spain was the tiny seaboard kingdom of Granada, facing Africa. The Catalans on the northeastern coast, like their forebears, the Carthaginians, are the natural business people of Spain, and have been in continual revolt against constituted authority from the earliest times. The recent revolution (1931) and their part in it, was inevitable and not surprising.

In the long struggle for a united, independent Spain, the Benedictine monks of Cluny, who came into Castile in 1033, were an important agency in activating the Catholic monarchs to the task of reconquest. There is no evidence extant of charitable medical aid in the Spanish medical cloisters before the advent of these Benedictines, who were the special creation of Charlemagne himself. In the cloister of Victoria and Emilia, there were books of medical recipes, like those of Western Europe in the 8th-9th Centuries, the oldest of these coming from the Pyrenean cloister of Ripoll, near Gerona, which was founded in 820 and existed up to the beginning of the 19th Century. Some two-thirds of these MSS. were found by Sudhoff[5] to be in the Royal Aragonese Archives at Barcelona. The oldest is a codex of the 8th-9th Century, comprising a recipe book, with therapeutic applications at the top of the page, an *Antidotarius* (collection of magistral formulæ) and a *Passionarius* (descriptions of diseases), with sundry Salernitan estrays. Some decades before the enfranchisement of the Ebro Valley, Toledo was already under home rule (1085). Its mosque was full of costly Arabic MSS. and it was soon to eclipse Cordova itself in medicine, philosophy and theology and as a center of social life. Here, then was the natural clearing house for Latin translations of the Arabized Greek texts of the Moors, of which the best came from Irak. The Latin paraphrase of the hygienic epistle of pseudo-Aristotle to Alexander by the Marano, Ibn Dawud or **John of Toledo**, became widely known all over the West and was dedicated to Princess Tharasea, daughter of Alphonso VI. About 1180, this fragment, enucleated from the *Secreta* of Aristotle, became the original of the *Regimen sanitatis* of Salerno. At this time, as shown by Steinschneider,[6] the Jews were the natural interpreters in these translating activities and the

[5]See his inventory of the MS. literature in *Spanische Forschungen d. Görres Gesellsch.* Münster i. Westfalen, 1930, II, 178-184.

[6]M. Steinschneider: *Die hebräischen Uebersetzungen des Mittelalters und die Juden als Dolmetscher.* 2 v. Berlin, 1893. *Die europäischen Uebersetzungen aus dem Arabischen.* Vienna, 1904-5.

Mozarabs were as helpful as the Jews. Arabic was actually spoken by learned Spanish Jews up to the 13th Century. This translating movement at Toledo, fostered by Archbishop Raimundo, Archdeacon Gondisalvo and others, eventually centered around Gerard of Cremona (1114-87), who came there from Italy to get a translation of Ptolemy's *Almagest* and thus started a school of translators which was active to the end of his life. Of 71 books translated under Gerard's direction, 28 were medical. Gerard is also said to have lectured in the Capilla de la Trinidad of the former Mesquita, but there is no evidence to this effect nor is any surviving MS. of Gerard to be found in the Biblioteca capitolar (Sudhoff). About 1212-14, Alphonso VIII of Castile founded the first Spanish university at Palencia, where a hospital had been established by the Cid in 1067. The University of Salamanca was founded by Alphonso IX of León in 1215, but not confirmed until 1243 (by Ferdinand III and later by a Papal bull of 1255). Universities were also planned at Lerida (1300) by Jaime II, at Valladolid (1346) and at Huesca (1354). In 1255, Alfonso X (the Wise) obtained from Alexander IV a bull founding an Academy of Medicine, at which Cordovan and Toledan physicians gave instruction based on the *Canon* of Avicenna and the *Colliget* of Averroes.

In the 12th Century, refuges were founded in Zaragoza for pilgrims, sick people and lepers. Similar institutions followed in many other cities. The leading medical figures of the time were the alchemist Ramon **Lull** (1235-1315) of Mallorca, who left an unpublished *Ars medicinae*, with astrological figures, now in the Library of the Escorial; **Arnold of Villanova** (1235-1315) of Catalonia, who wrote the famous commentary on the *Regimen Sanitatis* of Salerno, and Pope John XXI (**Petrus Hispanus**), who wrote on medicine (*Thesaurus pauperum*) and came to a tragic end at Viterbo in 1277. Sudhoff[7] states that the great Salernitan surgeon Theodoric, pupil of Hugh of

[7] Sudhoff: *op. cit.*

Lucca, may also have been a Catalan. Jean **Jasme** de Agramont (Johannes Jacobi) of Lerida wrote a pest tract in the Catalan dialect (1348), which bears some relation to the incunable of Johannes Jacobi or (Canutus) Klebs. Micer Johan, author of a *Llibre de receptes* was probably Juan de Valencia, physician to Alphonso I. A fragment of a medical MS. of 1381 by Estefano, physician to Bishop Don Pedro of Seville, is in Madrid (Sudhoff). Raimondo de **Sabunde** [-1432], of Barcelona, professor of medicine at Toulouse, was the author of *De natura hominis* (Cologne, 1501) and of a defense of Christian doctrine (*Theologia naturalis*), which Montaigne translated (1569) and defended in one of his Essays (II, 12).

The Fifteenth Century.

The period of struggle for national unity (1252-1479) was characterized by the ascendancy of towns and town life, the inevitable struggle between the principle of unification (vested in the King) and the decentralisation implied by the growth of power in towns and among the nobility, who, then as later, were "rich men" (*ricos hombres*) possessing broad estates (*latifundia*). The chief agents in this policy were Alphonso X (1252-84) called the Wise, and his great grandson Alphonso XI (1352-84). By the end of the 15th Century, the weak rulers who preceded Ferdinand and Isabella were apparently defeated, but, in reality, the power of the nobles was destroyed and monarchy was triumphant. At the same time, more power had been gained by the legislative bodies (*Cortes*) and the officialdom (*adelantados*) of the different capitals, and such Moorish survivals as the civil marriage (*á yurgas*) and the common law or bargain marriage (*barraganía*) were giving way to marriage by religious sanction (*benedición*). The legal obligation of proving that one's progenitors had no taint of Moorish, Jewish, heretic or infidel blood (*limpieza de sangre*) was not abolished until 1835.

During the 15th Century, **universities** were founded at Barcelona (1450), Zaragoza (1474), Mallorca (1483) and

Alcalá de Henares (1499), which, as being near Madrid, soon became a rival of Salamanca itself. It was richly endowed by Cardinal Ximenez in 1510, and three centuries later, was merged into the University of Madrid. In 1422, Juan II created a Tribunal of Alcaldes and Examiners to ascertain the competence of applicants for the right to practice medicine. The duty of examining physicians and surgeons to the king and the nobility was assigned to *protomedici,* of whom Alfonso Chirino and later Fernan Gómez were the first. These privileges of the "Protomedicate," dating from 1422, were confirmed by a law of March 30, 1477. So great were the privileges accorded physicians that they were protested against by the Cortes at Zamora (1432) and Madrigal (1438), but nevertheless reaffirmed by royal ordinances of 1435 and 1438, in virtue of which, no civilian or other authority could interfere with the business of the Protomedicate Tribunal. Spanish physicians, in fact, had a special tribunal of justice of their own from the start (1422), while the Royal Councils and Chancelleries of Valladolid, Madrid and Granada were not created until 1442, 1494 and 1505 respectively, the Council for the Indies in 1511 and the Tribunal of the Inquisition in 1483. **Insane asylums** (*casas de orates*) were founded at Valencia (1500), Zaragoza (1425), Seville (1436) and Toledo (1473). During the epidemic of plague in 1474, quarantine was established at Mallorca. Leper houses were established in great numbers and under direction of special officials (*alcaldes de lepra*). In 1240, Ferdinand III established a chair of **anatomy** in the University of Palencia, which was transferred to Salamanca by Alphonso the Wise. Dissection was done outside the city limits, usually in cemeteries. But progress in anatomy was not great and the physiology of the period was entirely Arabist. **Surgery** was in the hands of barbers, and Salamanca students practiced bandaging upon an articulated mannikin up to 1490, when Antonio Amiguet and Juan Vals established a school for technical instruction in surgery. The only text of consequence was a kind of hornbook of surgery in

rhyme (*Cirugia rimada*) by Diego Cobo (1412). Military surgery was forwarded by the service of **camp hospitals** and **ambulances** instituted by Queen Isabella during the expulsion of the Moors from Granada. Six large hospital tents were in evidence at the siege of Alora (1484) and four at the siege of Baza (1489). Wagons provided with beds appeared at the siege of Otrera (1477-8) and no less than 400 of these ambulances were employed after the capture of Malaga (August 19, 1487), as attested by Hernando del Pulgar (1484), Pedro Bosca (1487) and Peter Martyr (1489).

The materia medica of the New World was described by Diego Alvarez Chanca, who accompanied Columbus on his second voyage and by Rodrigo Fernández. Alfonso Chirino, physician-in-chief to Juan II, published in 1447 a MS. *Espejo de la Medicina,* which professed to standardize prescriptions but in reality exploited very complicated ones (Sudhoff). Of much more historic and bibliographic interest are the Spanish medical incunabula, catalogued by Konrad Haebler (1903-17) in particular the pest-tracts. The art of **printing** was introduced into Spain by the German Lambert Palmar, who published *Obres e trobes en lahors de la verge Maria* by Bernardo Fenollar at Valencia in 1474. The finest specimen of Spanish medical printing is probably the black letter translation of Lanfranc (*Cirurgia menor*), printed at Seville *por tres Alemanes compañeros* on May 15, 1495. As catalogued by Arnold Klebs, the Spanish **pest-tracts** are: the *Eclipse del Sol* of Diego de Torres (Salamanca, 1485), the *Regimen* of Luys Alcanys (Valencia, 1490), the *Aggregator* (Rome, 1499) of Pedro Pintor of Valencia, physician to the Pope Alexander VI; and the *Regimiento* of Fernan Alvarez (Salamanca or Barcelona, *circa* 1500). The Latin pest-tract of the Portuguese Valesco de Taranta (Padua, 1473) was translated into Spanish and printed at Barcelona (1475), Burgos (1495) and Pamplona (1495). The tract on syphilis by Gaspar **Torrella** of Valencia, physician to Alexander VI and Julius II, was published at Rome in 1497 and dedicated to Caesar Borgia, at that time Cardinal

Deacon of Valencia. It sounds an alarm over the accidents produced by salivation from mercurials, to which the death of Alfonso Borgia was attributed. In the second edition, printed at Blois (1499), small doses are recommended. Torrella, who afterwards became a Bishop, assisting at the Fifth Lateran Council, also wrote *Consilia* (1521) on the epidemic fever brought into Vizcaya in 1505 by the squadron of Flanders, which caused a mortality of 6000 in the northern province and spread all over Spain.

The Golden Age

The stretch of time covered by the reigns of Charles V and the three Philips (1516-65) is called by Spanish historians the *Siglo de oro,* their Golden Age. It was ushered in by such stirring events as the unification of Castile, León and Aragon under Ferdinand and Isabella, the conquest of Granada (1492) and the opening up of the New World by Columbus in the same year. In this period, Spain attained her height of military and naval prowess in Alva's campaigns, in the conquest of Mexico and Peru by Cortez and Pizarro and at the battle of Lepanto (1571). A little later, El Greco, Velázquez, Cervantes, Lope de Vega and Calderon gave her a position in art and letters second to none. The seeds of dissolution were already sown in the incursion of Ferdinand into Italy (1497) and the imperialist policies of Charles V and Philip II, which embarked the nation upon two centuries of meaningless wars, and depleted the enormous revenues derived from the colonies.[8]

In the 16th Century, Spain produced a number of physicians who were not without credit and renown among the anatomists, surgeons, obstetricians, medical scholastics and medical philosophers of the period. No less than Vesa-

[8]The annual revenues of Spain under Philip II have been estimated at 24 billion ducats or $360 billion, of which about one-half reached the national treasury, while the national debt left by the monarch was $1½ billion. By 1600, the revenues were about $270 billion, of which one-third was available, and the national debt in 1690 was still over a billion dollars. The purchasing power of these vast sums was far greater then than now.

lius was attached to the Spanish court from 1543 to the end of his life (1564) and Spanish anatomy was influenced by the *Fabrica* (1543) and its illustrations. Prior to Vesalius, Andrés **Laguna** (1494-1560), a medical graduate of Salamanca, who taught at Paris, Alcalá, Toledo and Bologna, published a book on anatomical method (dissecting) in 1535 and Luis **Lobera de Avila** a *Libro de Anatomia* (Alcalá, 1542). The chair of anatomy at Valladolid (*circa* 1550), the third in Europe after Bologna and Montpellier, was first held by Alonso Rodríguez de Guevara, a skilful prosector trained at Bologna, who did much to interest students in the subject and published a treatise at Coimbra in 1559. This was preceded by the *Anothomía del hombre* (Valladolid, 1550) of the Catalan anatomist, Bernardino Montaña de Monserrate, and followed by the well-known *Historia de la composición del cuerpo humana* (Rome, 1556) of

Juan **Valverde de Hamusco,** a pupil of Columbus and Eustachius at Padua, who became physician to Pope Paul IV. An Italian translation of this work was printed at Rome (1560) and reprinted at Venice by the Giunti (1586). A Latin translation of the explanation of the plates was printed by Plantin at Antwerp (1566) and reprinted by him in 1568, 1572 and 1579, as also a Dutch translation (Antwerp, 1568), reprinted at Amsterdam (1647). A complete Latin translation by Columbus was published by the Giunti (Venice, 1589) and reprinted in 1607. Italian translations of the Columbus version appeared at Venice in 1606 and 1682. The drawings, some of which derive from Vesalius, were made by the painter Gaspar Becerra and engraved by Nicolas Beautrizet, but as Choulant points out, the book contains several illustrations not in Vesalius. The description of the muscles of the eye is better, the small descending apophyses of the lumbar vertebræ are described for the first time and the nerves are conjectured to have a sheath, "like the bark of a tree."

From the Valencian school came Pedro **Gimeno,** a pupil of Vesalius (Padua) and Jacobus Sylvius (Paris), who published an exact description of the *stapes* as the "delta" (1549)[9], which brought him into violent controversy with another Valencian anatomist, Luis Collado, who defends his master Vesalius in a commentary on Galenic osteology (1555).

An important work on **artistic anatomy** (human proportion)was the *Varia commensuración* (Seville, 1585) of

[9]Pedro Gimeno: *Dialogus de re medica,* Valencia, 1549, cited by Garcia del Real.

the sculptor and goldsmith Juan de **Arfe** y Villafañe (1535-), of Leon, who acquired a great reputation as the fabricator of the hosts and other altar objects in Spanish cathedrals and churches. To this group of artist-anatomists belong also Alonso Berrugueste (1480-1561), Gaspar Becerra (1520-70) and Luiz de Costa (1599-), who translated Dürer's book on human symmetry into Portuguese. As **precursors of Harvey**, Lobera (1542), Sanchez Valdez de la Plata (1545), Bernardino Montaña de Monserrate (1551), Juan Calvo (1596) and the veterinarian Francisco la Reina (*Tratado de Albeitería*, Burgos, 1552), theorized about the circulation with an accuracy far in advance of their time and prior to Cesalpinus (1571-93) and the other Italian claimants.

Of the leaders of Spanish surgery in the 16th Century, the earliest and most important is

Francisco **Diaz**, a graduate of Alcalá who studied anatomy under Gimeno and Collado at Valencia, became surgeon to Philip II, published a surgical compend in the form of dialogues (1575)[10] and is memorable as the author of the first treatise on diseases and surgery of the urinary tract (1588)[11]. It contains an account of the high operation for stone, then called the Spanish method, as opposed to the "Neapolitan procedure" of Mariano Santo and explains the use of the urethral sound invented by Alderete.

Andrés **Alcazar**, of Guadalajara, a graduate of Salamanca where he subsequently held the chair of surgery, published a surgical treatise in 1575[12] and invented an apparatus for injecting or evacuating liquids into and from the chest.

Francisco **de Arceo** (1493-1575) graduated at Alcalá, and was a fellow student of the famous ecclesiastic philosopher Arias Montanus (1527-98), who also practised surgery and edited Arceo's posthumous work on the treatment of wounds (1576).[13] This book, which summarizes the experience of 45 years, was translated into English (by John Read, London, 1588), Dutch (1658, 1667) and German (Nuremberg, 1674). Arceo devised a balm called after him and a method of rhinoplasty highly praised by Sprengel, was against the stuffing of wounds with tampons, the abuse of sutures and the impalement of the cancerous breast in its amputation, but advocated bold trephining on occasion.

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[10]Francisco Diaz: *Compendio de cirugia.* Madrid, 1575.

[11]Diaz: *Tratado de todaslas enfermedades de los riñones, vejiga, carnosidades de la verga y orina.* Madrid, 1588.

Juan **Calvo**, a graduate of Saragossa and professor of medicine at Valencia, organized an Academy of Surgery in his own home, which drew many pupils. His surgical treatise of 1580,[14] was reprinted five times at Barcelona (1591), Madrid (1626, 1657, 1674) and Valencia (1690), and the section on ulcers was translated into French (Poitiers, 1596). He also published books on syphilis (1592), on internal medicine (1592) and a Spanish translation of the surgical treatise of Guy de Chauliac (Valencia, 1596).

Bartolomé Hidalgo **de Agüero** (1530-97) of Seville, was the first surgeon in Spain to teach the healing of wounds by first intention and became so skilful in wound surgery that duellists commended themselves "to God and the hands of Agüero." He was a voluminous writer, his most important surgical texts being his *Abisos* (1584) and his *Tesoro* (1604), both published at Seville. The latter contains the first Spanish treatise on the eye (*Historia del ojo*, 1586).

Juan **Fragoso**, of Toledo, was physician to Philip II and the author of two surgical treatises, viz., *Erotemas quirúrgicos* (Madrid, 1570) and a *Cirurgia universal* (Madrid, 1581; Alcalá, 1601). He also wrote a book on the officinal materia medica of Spain (Mantua, 1575; Madrid, 1583) and an account of East Indian medicinal plants (Madrid, 1572), a compilation from Garcia ab Orta, Monardes and Clusius, which was later translated into Latin by Israel Spach (Strassburg, 1601).

Dionisio **Daza Chacón** (1503-) of Valladolid, a surgeon in the armies of Charles V, was attached to the Military Hospital at Madrid (1557) and later to the Spanish fleet. He is said to have treated the wound of Cervantes at the naval battle of Lepanto (1574). His Surgical Practice (Valladolid, 1605),[15] reprinted at Madrid (1626) and Valencia (1650), describes his method of treating aneurisms and wounds of arteries by ligation. He was the first to recommend ligation of the tumor in the treatment of nasal polyps.

Perez **Lopez de León** worked under Agüero at Seville and later established himself in Cartagena, where he taught his master's methods. His principal work was a treatise on wound surgery (1628).[16]

All these surgeons were expert in trephining and each had his own particular technique in the treatment of such conditions as cancer of the breast and pleurisy. The first surgical publication to come from the New World was the rare and highly prized *Suma y recopilacion de cirugia* of Alfonso Lopez de Hinojoso (Mexico, 1595).

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[12]Alcazar: *Chirurgiae libri sex*, Salamanca, 1575.

[13]Arceo: *De recta curandorum vulnerum ratione*, 1575.

[14]Calvo: *Primera y segunda parte de cirugia universal*, Seville, 1580.

[15]Daza Chacón: *Práctica y teórica de cirugía en romance, y en latin.* Valladolid 1605.

[16]Lopez de León: *Práctica y teoría de las apostemas.* Sevilla, 1628.

The earliest Spanish works on the hygiene of pregnancy and infancy were those of Damian Carbón (Mallorca, 1541), Luis Lobera de Avila (Valladolid, 1551) and Juan Antonio de las Rueces y Fontecha (Alcalá, 1606). A defense of maternal lactation was published by Juan Gutierrez de Godoy at Jaen in 1529, and a book on children's diseases by Francisco Perez Cascales at Madrid in 1611.

During the 16th-17th Centuries, the bubonic plague ravaged Barcelona, Seville, Valencia, Zaragoza and Valladolid with heavy mortality and there was a goodly contribution to the tractate literature on this theme by Luis de Lucena (1523), Laguna (1542), Lobera de Avila (1542) and others.

Notable were the accounts of the epidemic at Zaragoza in May, 1564 by Juan Tomás Porcel (1565), which contains autopsy protocols; of the Valladolid epidemic by Ponce de Santa Cruz (1601); and of the outbreak at Seville in 1649 by Gaspar Caldera de Heredia (1650), all substantial contributions to the earlier literature of epidemiology. Among the syphilographers were Francisco **Lopez de Villalobos** (1496-), of Valladolid, who published the first poem on lues (*Salamanca,* 1498)[17] and *Las problemas de Villalobos* (1543); and Rodrigo Diaz Ruiz de **Isla**, whose tractate of 1542[18] first advanced the theory of American origin of the disease. In the delineation of typhus fever and diphtheria, Spanish physicians took the lead. The first account of *tabardillo* or endemic typhus came from the New World, in the *Opera medicinalia* of Francisco **Bravo** (Mexico, 1570), and was later elucidated in Spain through the monographs of Alonzo López de Corella, of Luis Mercado and of Luis de Toro, all published in 1574. There were six epidemics of diphtheria in Spain during 1581-1638 and the disease was first described by Casales, Fontecha and Villa Real in 1611. These three tracts were followed by a number of valuable epidemiologic studies, the most exhaustive of which were those of Alfonso Nuñez de Llerena (1615), Jeronimo Gil Pina (Zaragoza, 1636) and Pedro Miguel de Heredia (1665). Phthisis was elucidated in a chapter of the *Tribunal Apollini* (1568) of Cristobal **Pérez de Herrera**, hydrophobia in the valuable monograph of Juan Bravo (Salamanca, 1571), melancholia and epilepsy by Andrés Velázquez (1585). The first book on massage was the *Enchiridion* (Zaragoza, 1589) of Bernardino Gómez Mendes, Bishop of

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[17]Lopez de Villalobos: *El licenciado Villalobos sobre las contagiosas y malditas buvas.* Salamanca, 1498.

[18]Isla: *Tractado llamada Fructo de todos los Santos contra el mal serpentino venido de la Isla Española.* Seville, 1542.

Albarracin. The first work on the mineral waters of Spain was the *Espejo cristallino de las aguas de España* (Alcalá, 1697) by Ildefonso Limón Montero. The problem of unemployment and public charity was first handled in the *De subventione pauperum* (Bruges, 1526) of the celebrated humanistic philosopher Juan Luis **Vives** (1492-1540), who was imprisoned by Henry VIII for his defence of Catherine of Aragon, and who proposed first hand observation of nature *vs.* blind submission to the ancients a century before Bacon, and, with Paez de Castro, revived Herodotus' view that history should not be limited to a trite chronologic narrative, but should deal with every aspect of social life (*Culturgeschichte*).

Another great work of humanitarian endeavor was the method of teaching the deaf and dumb devised by the Benedictine Pedro **Ponce de Leon** (1520-84), which is preserved in the *Reducción* (Madrid, 1620) of Juan Pablo **Bonet**. The first book on spectacles was the *Uso de los antoios* of Benito Daça de Valdes (Seville, 1623).

The leading Spanish medical men of the Golden Age were Laguna, Mercado, Valles and Lobera de Avila.

Andrés **Laguna** (1499-1560), of Segovia, studied at Salamanca, Paris and Alcalá, graduated at Toledo (1539), accompanied Charles V on his campaigns in the Low Countries, rendered good service at the siege of Metz, renewed his studies at Padua (with Columbus) and Bologna, and became physician to Popes Paul II and Julius III. He discovered the ileocæcal valve, which is described in his compend of dissecting (1535),[19] published a pest-tract (1542), a system of dietetics for poor students and paupers (1547), a method of excising caruncles of the bladder (1543)[20] and a treatise on diseases of the joints, with a translation of the *Tragopodagra* of Lucian (1551), and was an industrious commentator of Galen (1551) and Dioscorides (1554). He wrote a life of Galen (1548) and an epitome of his writings (1551). His annotations on Galen were highly commended by Haller.

Luis **Mercado** (1525-1611), of Valladolid, whose portrait by El Greco hangs in the Prado, was physician to Philip II and Philip III, wrote on therapeutics (1572), malignant fevers (1574), diseases of women (1579), pulse (1584), institutes of medicine and surgery (1594), diseases of the liver, spleen, kidneys and bladder (1594)[21], practice (1604), hereditary diseases (1605), care and diseases of children (1611),[22] the nature of fever (1611). He also published one of the many Spanish accounts of plague (Madrid, 1599) and diphtheria (1614) and directions for the official examination of the *algebristas* or bone-setters (Madrid, 1599),[23] which was reprinted in Latin at Frankfort (1624). As a medical philosopher, his masterpiece was his *De veritate* (1604), for which he was called the Thomas Aquinas of medicine, a distinction hotly contested by Sprengel.

Francisco **Valles** (1524-92), of Covarrubias (Burgos), called the Spanish Galen and the "divine Valles," was a graduate of Alcalá (1553), who through

his commentaries on Hippocrates, Aristotle and Galen, did much to spread the taste for Greek medicine, as evidenced by the innumerable reprints of his learned annotations. Sprengel regards him as the ablest expounder of Arabic and Arabized medicine. He wrote on medical controversies (Alcalá, 1564), urine, pulse and fevers (Alcalá, 1569), therapeutics (Venice, 1589) and a tract on distilled waters (Madrid, 1592). His reputation as a medical philosopher is based upon his *Sacra Philosophia* (Lyons, 1588), a rational exegesis of the Bible.

Luis **Lobera de Avila**, who accompanied Charles V on all his campaigns and travels, is notable as the author of a book on personal hygiene and sterility male and female (Valladolid, 1551), which contains the first Spanish contribution to pediatrics. The original of this *Regimiento de salud* was published apparently before 1531, since it exists in a German translation of that date. The Spanish text of the pediatrics is surrounded by a garbled version of the Latin text of Bagellardo (Still). Avila also wrote on anatomy (1542), a pest-tract (*circa* 1542), a book on diseases of sudden impact (*De morbis subitaneis*) and one on the four diseases of courtiers, viz., catarrh, gout, stone (vesical, renal and hepatic) and syphilis (Toledo, 1544).[24] The section on syphilis recommends mercurial inunctions and was reprinted in Latin translation by Luisinus (1560).

Akin to Vives and Valles in spirit is the group of medical humanists and philosophers, of whom two surgeons,

Amatus and Zacutus Lusitanus, Isaac Cardoso (*Philosophia libera*, 1573), Rodriguez de Castro, Luis de Lemos and Francisco Sanchez (1552-) were of Portuguese Jewish origin, educated in Spain.

Of this group, Antonio Gomez Pereira (1500-) was such an effective opponent of Galen, that his masterpiece, the *Antoniana-Margarita* (Medina del Campo, 1554) was almost entirely destroyed by perfervid Galenists. A pioneer work in pedagogics, phrenology, and vocational aptitude is the *Examen de ingenios para las ciencias* (1557) of Juan de Dios Huarte y Navasco. The *Nueva filosofía* (Madrid, 1587), an analysis of human passions which passed through many editions, is attributed on the title-page to Doña Oliva del Sabuco, but was really written by her father, Miguel Sabuco y Alvarez.

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[19]Laguna: *Anatomica methodus.* Paris, 1535.

[20]Laguna: *Methodus cognoscendi extirpandique nascentes in vesicae collo carunculas.* Venice, 1543.

[21]Mercado: *De jecoris, splenis, renum et vesicae morbis, eorumque curatione.* Madrid, 1594.

[22]Mercado: *De morbis puerorum,* Valladolid, 1611. *De puerorum educatione, custodia et providentia.* Valladolid, 1611.

[23]Mercado: *Instituciones que su Magestad mando hazer al Doctor Mercado para el aprovechamiento y examen de los algebristas.* Madrid, 1599.

[24]Lobera de Avila: *De las quatro enfermedades cortesanas.* Toledo, 1544.

The *Restitutio Christianismi* (Vienne, 1553) of Miguel Servede or Servetus (1509-53), of Villaneuva (Aragon) contains his memorable account of the pulmonary circulation.

From the New World came the description of its plants in the *Sumario* (Toledo, 1525) of Gonsalvo Ferdinando de **Oviedo** y Valdez (1478-) and the *De las drogas de las Indias* (Seville, 1565) of Nicolas **Monardes**. The mountain sickness of the Andes was described by the Jesuit traveller José **d'Acosta** (1540-99), of Medina del Campo, in his *Historia natural y moral de las Indias* (Seville, 1590), which was translated into English (London, 1604). The medicinal plants of the East Indies were described in the *Coloquio dos simples e drogas* (Goa, 1563) of the Portuguese naturalist Garcia de **Orta** and the *Tratado de las drogas* (Burgos, 1578) of Cristobal **Acosta** (-1580).

During the 16th Century, universities were founded at Valencia (1500-1), Santiago (1504-26), Seville (1502), Toledo (1518), Granada (1531-7), and Oviedo (1574, opened 1608). In the 17th Century, Fernández de Navarrete records that there were 34 universities in Spain.[25]

The University of Madrid was slowly evolved from the Colegio de Doña Maria de Aragon, founded in 1590, and ultimately fused with the ancient university of nearby Alcalá in 1836-7.

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[25] As far as ascertainable, these were at Palencia (1212-14), Salamanca (1215-43), Huesca (1255-1354), Lerida (1300), Valladolid (1346), Barcelona (1450), Siguenza (1472), Zaragoza (1474), Avila (1482-1807), Mallorca (1483; 1697), Alcalá de Henares (1499), Valencia (1500-1501), Seville (1502), Santiago (1504-26), Osuna (1515), Toledo (1518-20), Granada (1531-7), Lucena (1533), Bueza (1533; 1565), Sahagún (1534), Oñate (1542), Gandía (1547), Osme (1551), Almagro (1553), Oropesa (1553), Orihuela (1568), Tarragona (1572), Oviedo (1574; opened 1616), Vich (1599), Pamplona (1608), Gerona (1617), Solsona (1617), Tortosa (1645) and Irache. By the legislative reforms of 1857, these were reduced to 10 university districts, viz., Madrid, Barcelona, Granada, Oviedo, Salamanca, Santiago, Seville, Valencia, Valladolid and Zaragoza. On account of the long intervals between the successive charterings by Popes or Emperors, the subsequent dates of reorganization *longo intervallo* and other details, it is impossible to assign definite dates of origin to many of the mediæval and Renaissance universities. But many of the Spanish universities, little known to the historian, e.g., those at Oñate (Guipúzcoa), Baeza or Tortosa, were ornate structures of magnificent architectural design.

In the 17th Century, Spanish poetry, fiction and painting rose to a great height through the work of Lope de Vega and Velázquez (both born in Madrid), Cervantes (Alcalá) and Velázquez (Seville). Cervantes and Velázquez are related to medicine with reference to the depiction of border-line mental states: Cervantes through his moon-struck knight, Velázquez in his representations of achondroplasic, cretinoid, hydrocephalic and rachitic dwarfs and of idiocy. To this group of paintings belongs also Ribera's paralytic boy (Vienna Gallery) and Careño de Miranda's representation of endocrine obesity (Prado).

The great Spanish tradition in **bibliography** started with the *Bibliotheca hispana nova* (1672) *et vetus* (1696) of Nicolas **Antonio** (1617-84) of Seville, a tradition which was to be fruitful of colossal achievement in the Western Hemisphere and rivalled by the work of the Spanish cartographers only.

In the so-called *Geisteswissenschaften,* the writers of the 16th-17th Century Spain, were not only original but influential. In international law, Vitorio and Vázquez antedated Grotius, who acknowledges his debt to them. The *Política Indiana* (1629-39) of Solórzano was a great treatise on colonial government and finance. Long before Adam Smith, Martinez de la Mata announced that labor is the only true source of wealth, and the Proudhon-Soviet doctrine of the control and redistribution of private property by the state was ancient history to Luis Vives. Juan Páez de Castro (died 1570), chronicler to Philip II (1555), not only recommended that the king start a library in the Escorial,[26] but began it by donating his own collection of rare books and codices. His *Memorial de las cosas necesarias para escribir historia,* posthumously printed, formulates the program of the modern social, cultural and psychologic historian. The *Brevissima Relación* (Seville, 1552) of the colonial evangelist Bartolomé de las Casas

[26]Páez de Castro: *Memorial sobre la utilidad de juntar una buena biblioteca.*

(1474-1566), which files his famous protest against cruelty to the Indians of the New World, is a humanitarian document of the first order.

The Period of Decadence (1700-1800)

With the accession of Philip V (1700-1746), grandson of Louis XIV, the Hapsburg dynasty came to an end and the Bourbon began. The Spanish monarchs of the 18th Century were a series of "enlightened despots," whose able ministers and financial advisers tried to avoid war, where possible, and were thus able to recoup the depletion of the national treasury by reforms and economies, which brought about an interlude of relative prosperity, until the whole edifice was thrown to the ground again by the ruthless policies of Napoleon. Gibraltar was lost to England by the war of the Spanish succession (1700-13) and Philip V, under the sway of his second wife, Isabel Farnese of Parma, was again involved in expensive intrigue for Italian dominions; but he had the good sense to leave finance (*hacienda*) to the able Jean Orry, as did his successor, Ferdinand VI (1746-59) with his ministers, Enseñada and Wall. The same policies were pursued by Charles III (1759-88), the most enlightened of the group, who was guided by such strong and stable advisers as Aranda, Campomanes and Floridablanca. When the inept and sluggish Charles IV (1788-1808) dismissed Aranda and Campomanes in favor of Manuel Godoy, the trivial lover of Maria Louisa, the time was ripe for the political chaos and bloodshed of the Napoleonic period, with the long sequel of misrule, palace intrigues, insurrections and Carlist wars which followed up to the accession of Alphonso XIII. The maritime power of Spain was broken at St. Vincent and Trafalgar and her military power by Napoleon. Her South American colonies acquired independence one by one and were protected from European intervention by the Monroe Doctrine (December 2, 1823) and the support given the principle by George Canning in the House of Commons. Thus Spain lost colony after colony, and the relative prosperity engendered by the shrewd finan-

cial policies of her able ministers was again dissipated by the expenses of another century of senseless warfare and the equally wasteful expenditures of the court. The poverty and misery of the people engendered continual revolt and the invasion of the country by foreign soldiery initiated a carnival of rape and virtual murder of defenceless civilians. The ablest Spaniard of the time would seem to have been the great painter Goya, who satirized the contemptible spirit of the period with merciless precision. But a new spirit arose when the people of Spain revolted in mass against Napoleon, who was thrown out of the country as much by this guerilla warfare as by Wellington's infantry. The battle of Vittoria (1813), which anticipated Leipzig (1813) and Waterloo (1815), was regarded as so momentous in Central Europe that it was celebrated by a symphonic overture of Beethoven, played at the Congress of Vienna (November 27, 1814). The intrigue of the Spanish marriages and the subsequent reign of Isabella II (1843-68) was a prolonged political farce, and the loss of the Spanish Antilles and the Phillipines in the Spanish American war (1898) proved to be the term and end of decadence and ushered in the dawn of a new day. The uprising of the whole people of Spain against the tyranny of Napoleon on May 2, 1808 (*Dos de Mayo*) is now celebrated annually as their Independence Day.

Thus, even before the Golden Age, the germs of decadence were sown when Ferdinand of Aragon embarked upon the perilous policy of invading Italy for prestige and domination (1497). The defeat of the Invincible Armada (1588) and of the hitherto invincible Spanish infantry at Rocroy (1643) were already premonitory of Trafalgar. Yet to the middle of the 17th Century, Spain held her own fairly well in respect of intellectual production, while her period of decadence, although one of relative financial prosperity, was characterized by a creditable array of representatives in all branches of science, the fine arts and industry, none of whom had any decisive effect upon European culture except the great painter Goya, certain geog-

raphers and cartographers, and Manuel García, the teacher of singing who invented the laryngoscope (1855).

The 18th Century was a period of reform in medical education and public health administration as well as in finance and government.

An epidemic of plague in 1720 led to the formation of a National Board of Health (*Junta suprema de salud*), which was suppressed in 1740 and 1805, to be revived in 1743 and 1807 and reorganized in 1847. Close upon the expulsion of the Jesuits (1767), certain reforms in university reorganization were instituted, which resulted in better anatomical teaching at Granada (1777) and Valencia (1787). In this period, the status of anatomy, surgery and clinical medicine has been regarded by the Spanish medical historians as deplorable. In 1748, the first *Colegio de cirugía in Spain* was opened at Cadiz, another was created by royal mandate at Barcelona in 1760 (opened 1764), and a third at Madrid in 1778 (opened 1787). By a royal order of March 16, 1795, two chairs of clinical medicine were established in the Hospital general at Madrid, and similar courses were instituted at Valencia (1787) and Barcelona (1797). The Royal Spanish Academy was founded at Madrid in 1713 and the *Real Academia Nacional de Medicina* in 1733. The **first Spanish medical periodical**, the *Efeméride baromètrico-médicas matritenses* (1734), was the literary organ of this Academy. Its title emphasies the attention paid to medical meteorology by the 18th Century physicians. The Museo nacional de ciencias naturales (Madrid) was founded in 1771.

With reference to consequential position in the general history of European medicine, the leading Spanish physicians of the period of decadence were Gaspar **Casal**, who first described pellagra (*mal de la rosa*) in his *Historia Natural y Médica del Principado de Asturias* (1762); the surgeon Antonio **Gimbernat** (1734-1816), who, in 1768, devised a new operation for femoral hernia turning upon his discovery of the ligamentous structure in the crural arch which goes by his name; and the toxicologist Mateo José **Orfila** (1787-1853), of Mahon (Minorca), who studied at Valencia and completed his medical education in Paris, where he became Dean of the Paris Medical Faculty (1830), published well-known treatises on toxicology (1813-14), medical chemistry (1817), first aid (1818) and medical jurisprudence (1823-5) and played a leading and sometimes dramatic rôle in the trials and poisoning episodes of his period. Gimbernat, in 1768, also discovered

the Clocquet ganglion in the femoral ring, which he demonstrated to John Hunter in 1775 and described fully in 1793. In 1777, when Hunter was dilating on the dangers, incident to operating for femoral hernia, Gimbernat demonstrated to him his new method, which won from the Scotch surgeon the commendation: "You are right, sir. I will describe it in my lectures and will use it whenever I have occasion to operate on the living."

Of more local prominence and importance in the advancement of the national medicine was Pedro **Virgili** (1699-1776), the principal reformer of medical education in 18th Century Spain.

The son of a humble Catalan farmer, Virgili tilled the fields up to the age of 14, when he got a position as a barber-surgeon in the hospital at Tarragona, and after three years experience with venesection, proceeded on foot to Montpellier to begin his medical education. Here he devoted himself mainly to dissection and completed his studies in Paris. Returning to Spain, he was made Chief Surgeon of the Tarragona Hospital and a little later surgeon to the Royal Navy. He played a prominent part in the actions off Gibraltar and Oran and his account of a successful tracheotomy in the hospital at Cadiz was deemed worthy of publication in the Memoirs of the Royal Academy of Surgery at Paris (1743). He became physician to Ferdinand VI, which gave him his opportunity. At this time, the Spanish Navy was manned by foreign surgeons and when the Marquis de Enseñada decided to enlarge the fleet, Virgili laid his plans to set off this deficiency by the foundation of a College of Surgery for the Navy. He chose Cadiz, where he had a building constructed with complete laboratory and surgical equipment, at the same time sending medical students of unusual aptitude to Paris, Bologna, Leyden and London. In two years time (1748), his College of Surgery was opened with a personnel of 12 professors and 50 salaried internes, who were later increased to 100. The institution was in fact a surgical seminary, which became so successful that Virgili in 1758 secured royal permission to erect a similar College for Army Surgeons at Barcelona, which was completed and opened six years later (1764). Here fifty graduate internes were trained annually and to relieve the institution of any dependency upon the University or medical officialdom, it was put under the military command of the Captain General of Cataluña. This was the Declaration of Independence of Spanish surgery. From 1764 on, the medical confraternity of SS. Cosmas and Damian was forbidden to license surgeons. The most distinguished interne of the College at Cadiz was Gimbernat, who was entered in 1758 and, at Virgili's instance, was made professor of anatomy there in 1762.

Nearly forty years intervened between the opening of the College of Surgery at Cadiz (1748) and that at Madrid (1787) but in this period there was marked improvement in the quality of Spanish anatomy and surgery. The medical celebrities of the first half of the century were either confirmed hide-bound Galenists or closet anatomists, who did no dissecting.

Of the older dispensation were Solano de Luque (1685-1738), author of *Lapis Lydius Apollinis* (1731), a Galenic consideration of the varieties and subvarieties of the pulse; Martin Martinez (1684-1734), a highly cultured physician who was aware of the deficiencies in medical education and incurred bitter enmity by attempting to correct them, but whose *Noches anatomicas* (Madrid, 1723-50) and *Anatomia completa* (Madrid, 1730) is regarded by the Spanish medical historians as far inferior to the work of Valverde de Hamusco; Francisco Lloret y Marti, an exaggerated Galenic astrologer, who held the chair of anatomy and mathematics at Valencia for twelve years but wisely gave it up to become a titled functionary in Bilbao; and Andres Piquer (1711-72), who held the same chair at Valencia in 1742-51, during which time he devoted himself to the composition of books on physics (1745), and logic (1747) but ignored anatomy. He was a talented polyhistorian, whose treatise on fevers (Valencia, 1751-77) was translated into French and whose trilingual anthology of Hippocrates (Madrid, 1757-81), giving the Greek text with Latin and Spanish translations, was even more highly esteemed.

Of more scientific importance were

José **Quer y Martinez** (1695-1764), an army surgeon who revived Spanish botany in *Flora española* (1772), whom Linnaeus honored by naming the genus *Queria* after him and who wrote a pamphlet on the treatment of renal colic with uva ursi (1775); José Alsinet who wrote on the use of quinine in paludism (1774); the medical mathematician Antonio **Capdevila**, who corresponded with Haller and furnished him the Spanish data for his bibliographies; and two students of yellow fever, viz., the highly educated and combative Ignacio Maria Ruiz **Luzurriaga** (1736-1822) and José **Masdevall**, inspector general of epidemics in Catalonia, whose *Relacion de las calenturas putridas* was published in 1784-6.

The stimulating effect of the three colleges of surgery is sensed in the work of such men as

Leonardo **Galli**, author of a monograph on fractures of the patella (1795); Queralto and Rives, professors of surgery in the Madrid College; Jaime **Bonells** and Ignacio **Lacaba**, whose treatise on anatomy (1796) became the standard text-book in Spain for nearly half a century; Diego **Velasco** and Francisco **Villaverde**, whose treatise on operative surgery (1780) enjoyed

an equal popularity; Francisco Salvat y Campillo (1751-1828), champion of variolation and student of scurvy and yellow fever; Pedro María González (1763-1837) author of a treatise on naval medicine; Juan Palarea, called *el Medico,* who became a colonel of guerillas in the uprising against Napoleon; and the medical historian Antonio **Hernández Morejón** (1773-1836), who also served as a medical officer in the Army.

The Nineteenth Century

The first notable achievement in the 19th Century was the introduction of **vaccination** into Spain by Francisco **Pigillem**, who vaccinated three children at Pingcerdá in December, 1800.

He was followed by Gil y Albeniz in Rioja (1801), Pedro Martin in Cadiz, Luzurriaga and Zunzunegin in Madrid and Hernández Morejón in Valencia. It was then decided to carry the method to the New World. An expedition, headed by Francisco Xavier **Balmis** (1753-1819) was organized by a royal mandate of June 6, 1803 and carried the practice to all the Spanish possessions in the New World and in Asia. In Cuba, it was found that vaccination had already been introduced by Tomás Romay, but Balmis drew up the plan for a Central Vaccine Station (*Junta central de vacuna*) in the island. Upon his return, he was made Inspector General of Vaccination in Spain and the Indies and devoted the rest of his life to this detail. He published a book on the medicinal virtues of the roots of the agave and begonia (1794), which was translated into German (1797).

Prominent among the medical reformers of the early period were

Pedro Castelló y Ginestá (1770-), professor at the College of San Carlos (1801) and physician to Ferdinand VII (1825), who was influential in bringing about the reforms in medical education of 1827 and the laws creating the Junta Superior regulating medical practice, the reforms in the army medical service, the mineral baths and the Academy of Medicine.

Pedro **Mata** y Fontanet (1811-73) of Reus (Tarragona) was imprisoned and twice banished for his political activities, coming under Orfila in Paris, and finally settling down as a government official in Madrid (1843-54), where he drew up plans for reforming medical education which were hotly discussed. He was again active in the September revolution of 1854, which brought him important preferment. He was professor of legal medicine in the Madrid Faculty and his most important work is his treatise on the subject (1844), which passed through five editions. Mata was a temperamental doctor, author of several novels, one of which (*Eloisa y Abelardo*) was suppressed.

Mateo **Seoane** (1791-1870) was driven by his political activities to spend the greater part of his life in England, where his services to public hygiene,

in particular during the cholera epidemic, were such that he was liberally recompensed by the government and admitted to the London Society of Medicine, the Royal Institute of Great Britain and the Royal College of Surgeons. He founded the London *Athenaeum* and compiled the well-known Spanish-English Dictionary (1830) which is still used: Returning to Spain in 1834, he drafted the prospective sanitary legislation of 1837 and during the remaining thirty years of his life, there was no advance in education, public hygiene or social welfare of which he was not the principal prime-mover.

The most active propagandist for the study of public hygiene was Pedro **Monlau y Roca** (1808-71) of Barcelona, who served in the army (1833-47), the Board of Health (1847-71) and came to the chair of hygiene in the Madrid Faculty in 1854. His principal contributions were treatises on public hygiene (1847), marital hygiene (1853) and industrial hygiene (1856), and a number of humorous writings, such as his one-act comedy on quackery (*Lo que es un curandero,* 1830).

The Spanish **anatomists** of the 19th Century derive from the famous text-book of Bonells and Lacaba (1790), which was in use up to 1850, and from the dissections of Gimbernat and Lacaba in the Colegio de San Carlos (Madrid). From Gimbernat stemmed the long line of anatomists and surgeons of the Madrid Faculty:

Up to 1830, Argumosa, Castelló, Roca y Gutierrez and Hisera; during 1840-60, Sanchez Toca, Corral, Viñals, Fourquet; and in the later period Martinez Molina, Villanueva, San Juan, Creus, Velasco and Calleja; in Granada, San Juan Oloriz, Creus, Ribera; in Valladolid, Calleja and Salvino Sierra; in Valencia, Llobet, Zurriaga, Gomez; in Barcelona, Letamendi; in Cadiz, Rubio y Gali, who taught the Dominguez, Amettlers and Benjumedas; in Santiago, Freire, Teyero and Romero Blanes; in Zaragoza, Vega y Lozano and Cajal.

Of this line of apostolic succession from Gimbernat to Cajal, the most remarkable were

Federico **Rubio y Gali** (1827-1902), who made his modest dissecting room at Cadiz famous for accurate and solid practical work; Juan **Fourquet** (1807-65), of Madrid, who came to the Madrid chair in 1848, discovered the stylo-auricular muscle, corrected many errors in classical anatomy, particularly of the locomotor and vascular systems, made a topographical chart, created the Iconographic Museum of the Madrid Faculty (1853), and left his modest fortune to establish an annual anatomical prize of 500 pesetas for second year students; Pedro Gonzales de **Velasco** (1815-82), who neither discovered nor wrote anything, but impoverished himself by squandering his immense fortune of 3 million reales on the erection of a Museum of Anthropology (1875)[27] and Medical Studio for the Madrid

Faculty. He has been canonized in a biographical eulogy by his pupil, Angel Pulido (1894); Federico **Olóriz** y Aguilera (1855-1912) of Granada, who founded the Craniological Museum in the Madrid Faculty, containing 2,250 skulls with complete authenticated data in each case, published studies on the geographic distribution of the cephalic index, based on 8,368 measurements (1892), on height (1896), longevity (1898) and illiteracy (1900) in Spain, and a manual for the identification of delinquents (1911); José de **Letamendi** y Manjarrés (1828-97) of Barcelona, who wrote on criminology (1883), origins of handwriting (1885), a Course of General Pathology (1883-9), a Course of General Clinics and who was also a versatile painter and musician and composer of a requiem mass, which is sung in the Monastery of the Escorial. Julian **Calleja** y Sanchez (1836-1913) a pupil of Fourquet, taught successively at Granada, Valladolid and Madrid, and wrote several anatomical text-books, including treatises on myology (1872), angiology (1877) and embryology. Marcos **Viñals** (1812-95), of Burgos, demonstrated the origin and course of the chorda tympani in a unique preparation of the internal ear (1841).

The Spanish **surgeons** of the 19th Century make a long list. Spain claims priority for Romero in pericardiotomy (1819), for Rubio y Gali in the Halsted operation for cancer of the breast, for Argumosa (1832) over Dieffenbach (1834) in the performance of blepharoplasty and for parotidectomy without previous ligation of the external carotid (1834); for Ribera (1878) over Estlander (1879) in resection of the ribs for pleurisy (Gustav Simon, 1869), and over Momburg in the use of the abdominal hæmostatic ligature.

At the head of the modern group, García del Real signalizes

Alejandro **San Martin** (1847-1908), professor of pathology and clinical surgery in the Madrid Faculty, who devoted the last decade of his life to the study of experimental vascular anastomosis. A case of extensive gangrene of the foot from obliterative endoarteritis suggested to him the possibility of relieving the obstruction by arterio-venous anastomosis. He

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[27] In this grandiose undertaking, poor Velasco was fleeced by unscrupulous contractors, lost his chair and clientèle, and when at last, reduced to penury, he tried to persuade the Madrid Faculty to purchase his museum, he was snubbed with the inevitable come-back: "Nobody asked you, Sir, she said." Ignored by old friends and patients, he was driven to accept the simple charity of humbler people. This trait of meridional Quixotism, charming in itself, illustrates the shrewd observation of Lord Bacon that the Spaniard is "seeming wise." Another hobby horse was the continuation of the *faire la guerre* policies of Charles V and Philip II.

performed 40 experiments on 36 dogs, then tried out his method in two cases of gangrene of the foot (1902), but without evading the necessity of amputation. His work was, however, in the new trend of vascular surgery continued by his pupil Goyanes, Jaboulay, Carrel, Wieting and others. In 1898, San Martin devised a method of amputation at the hip-joint.

The leading surgeon of the early period was Diego de **Argumosa** y Obrégón (1792-1865). In his *Resumen de cirugia* (1856) he described and recommended phleborraphy as a substitute for ligation of the veins, although he never attempted the operation himself. Argumosa devised methods of cheiloplasty, perineal urethrostomy (Poncet) and amputation of the hip, excised the parotid gland (1832), the tongue (1835), excised the penis for cancer (1845) and in 1832 performed blepharoplasty. His priority was disputed by Joaquin Hysern (1804-83), who claimed that he had done the temporo-faciai operation with success in 1829 and 1833.

At Granada, José **Ribera** y Sans (1852-1912) employed, as stated, the Momburg elastic ligature of the abdomen for hæmostatic purposes, is credited with resection of the ribs for empyema (1878), made a study of 117 cases of hydatids (1908) and devised original methods of trephining (1898), posterior mediastinotomy (1899), total gastrectomy (1902-11), interilio-abdominal amputation (1908-11) and paraperitoneal laparotomy (1908), also a theoretical approach to the pituitary (1910).

Federico **Rubio** y Gali (1827-1902) founded the surgical institute (*Instituto de terapeutica operatoria*, 1880), or Instituto Rubio in the Hospital de la Princesa on the heights of Moncloa (Madrid), was the first surgeon in Spain to perform ovariotomy (1860), hysterectomy (1861), nephrectomy (1874) and laryngectomy (1878), and turned out among his pupils such specialists as Ariza (oto-rhino-laryngology), Svender (genito-urinary surgery), Buisen (neurology) and Gutierrez (gynæcology).

Eugenio **Gutiérrez** y González (1851-1914) was the founder of gynæcology in Spain. He became gynæcologist to the Rubio Institute in 1881 and contributed to all phases of the subject. He was also an able obstetrician and was summoned to deliver the Queen in May, 1907. Another pioneer in gynæcology was Miguel Angel **Fargas y Roca** (1858-1916), who performed the first ovariotomy for cyst (1882) and the first gastro-enterostomy (1895) in Spain.

Salvador **Cardenal** (1852-1927) of Barcelona, was the pioneer of antiseptic surgery in Spain and author of a book on the subject (*Cirugia antiséptica*, 1880).

Juan **Creus** y Mansó (1828-97), like Argumosa, devised methods of cheiloplasty and amputation at the knee-joint (1885).

Melchior **Sanchez de Toca** (1806-80) performed abdominal hysterectomy for uterine tumor (1845), and in the same year, another Spanish marquis, Tomas **Corral** y Oña (1807-82) is said to have performed the vaginal Cæsarean operation introduced by Dührsen in 1898. Priority over Billroth

(1889) and Jaboulay (1894) is claimed for Felipe **Margarit**, of Barcelona, in the performance of the interilio-abdominal amputation at the hip-joint (1888).

The leading **obstetricians** of the period were

Francisco **Cortejarena** y Aldebó (1835-) and the Marquis Andrés del **Busto** (-1899), editor of *España Médica* (1856-66), the organ of the Academy of Surgery, and founder of *Iberia médica* (1857-8).

Prominent also among the **medical journalists** were

the reformer Rafael **Rodríguez Mendez** (1845-1919), rector of the University of Barcelona (1901), who founded the *Gaceta médica catalaña* (1881) and organized the first Spanish Congress of Tuberculosis (1910); Francisco **Mendez Alvaro** (1806-83), founder of the *Boletin de medicina y farmacia* (1834-5) and editor of its successor, *Siglo médico* (1854-83); Matias **Nieto y Serrano** (1813-1903), who founded the *Boletin mensual de novedades médicas* (1841), which became the *Gaceta médica* in 1842, with Fourquet as co-editor, and ultimately fused with the *Boletin de medicina, cirugia y farmacia* (1834-54) to form the *Siglo médico* (1854); and Antonio Valázquez de Castro (1840-) founder of the *Presna médica de Granada* (1879), which became in 1882 the *Gaceta médica del Sur de España.*

Among the earlier **clinicians**, a notable Triton among the minnows was

Vincente **Asuero** Cortazar (1807-73) author of *Terapeutica substitiva* (1850) and reputed to be the leading Spanish physician of his day. The outstanding internist of the later period was Maximo **Teijéro** (1827-1900), who translated several books and was detailed by the king to report on Pasteur's treatment of rabies in 1886. A pioneer in **dermatology** was Benito **Hernando** y Espinosa (-1916), memorable for his self-sacrificing labors during the cholera epidemic of 1885 and his massive report on leprosy in Granada (1884), which drew both Virchow and Neisser to the city. The onstanding authority in dermatology in Spain was José Eugenio **Olavide**, author of a great treatise in three volumes (1871-80) and of clinical studies on the herpetic and rheumatic dermatoses. In the field of diseases of the ear, nose and throat, Ramon de la **Sota** y Lastro (1834) founded the *Instituto de otorhinolaryngologia;* Ricardo **Botey**, author of clinical studies (1891-3) and a textbook (1902), founded the international *Archivos* (1890) devoted to the subject; Vincente **Llorente** y Matos (1857-1916), founded the Instituto Llorente (de microbiológia y seroterapia, 1894), was the first to perform intubation of the larynx in Spain (1896-7), analyzed 3500 cases of diphtheria (1904) and did experimental work on tissue cultivation with Carrel at the Rockefeller Institute (1913). A. Garcia **Tapía** made a notable contribution to **neurology** in his account of partial right-sided and total left-sided hémiplegia allocated to a lesion in the medulla (1905). A similar contribution was made by the ophthalmologist J. A. **Barraquer** of Barce-

lona, who first described progressive lipodystrophy (1906) and devised the well-known procedure for extracting cataract (phakoeresis, 1917). Cayetano del **Toro**, once a gynæcologist, went over to ophthalmology and became editor of the *Cronica oftalmologica* (Cadiz, 1873-83). Rafael **Cervera** (1828-1903) founded the Casa de misericordia de Santa Isabel (1857) and became director of the Instituto oftalmologico founded by Delgado Jugo. Rodolfo de **Castillo** (1850-) devised a new method of resecting the inferior maxilla (1889) and made a study of Roman ophthalmology (1905), which was translated by Max Neuburger (1907). Of the physiologists, **Pi y Suñer** and Ramon **Turro** were outstanding in Barcelona, and José Gomez **Ocaña** (1860-1919) in Madrid. A pioneer in **pediatrics** was Mariano **Benevente** (1818-85). In the later period, Manuel **Tolosa Latour** (1857-1919) was editor of several pediatric periodicals, translated many foreign books, and founded the seaside sanitarium for tuberculous children at Chipiona, near Cadiz (1897). Among the psychiatrists, José Maria **Esquerdo** (1842-1912) played a gallant part in the cholera epidemics (1865, 1885) and the Carlist wars (1874), founded the famous asylum (Manicomio) at Carabanchel (1877) and was a member of the Cortes during 1893-1900. In medical jurisprudence, criminal anthropology and morbid psychology, the Spaniards, like the Italians, have done good work, in particular Lecha Marzo, Bernardo de Quirós and José Ingegnieros (1877-1925). Antonio **Lecha Marzo** (1888-1919), a medical officer of the Spanish Army (1911), who held the chair of legal medicine at Seville (1914) wrote on such themes as finger prints and scientific palmistry (1912), medico-legal microchemistry and such like, and died prematurely, leaving an unfinished textbook. A precursor of Ramón y Cajal in neurohistology was Luis **Simarra** y Lacabra (1851-1921) founder of the Spanish Association for the Advancement of Science, who held the chair of experimental psychology in the Madrid Faculty. He left his entire fortune and estate, including his splendid library, to the project of founding an Institute of experimental psychology at Madrid. Finally, let mention be made of the dramatist, José Echegaray (1832-1916), whose remarkable plays, often dealing with pathologic and psychiatric themes, won him the Nobel Prize in 1905.

Important reforms in **medical education** and **sanitation** were effected by the Royal Decree of July 4, 1827, uniting the Spanish medical faculties under a single Junta, the plan of Pedro Mata for further reorganization of medical education, confirmed by a Royal order of October 26, 1843, and corrected by the legislation of 1847, which centralized higher public instruction in ten universities, controlled by a Minister of Education, with medical faculties of the first class at Madrid, Barcelona and Cadiz, and of the second class (five year courses) at Valencia, Santiago, Salamanca and Granada. All this was further modified by leg-

islation of 1849-61, up to the law of October 25, 1868. Many mediæval formalities and red-tape obstructions to progress were abolished in the sanitary legislation (*ley de sanidad*) of November 28, 1855.

In **medical history** Spain has a record of very solid performance, as also in **bibliography**, from Nicolas Antonio to Menéndez Pelayo and the achievement of Toribio Medina in Latin America. Of the medical historians,

Antonio Hernández **Morejón** (1773-1836) and Anastasio **Chinchilla** y Piqueras (1801-67) were army surgeons, and Chinchilla, in particular, rendered valiant service in the Carlist insurrection of 1835. Morejón's posthumous *opus magnum*, a Bibliographic History of Spanish Medicine (1852), was published by his literary executors Juan Gualberto Aviles (1799-1865) and Chinchilla, in whose arms he expired in his last illness and who was later accused of ingratitude toward the master by his bitter rival, Aviles. Chinchilla's principal performance is his *Anales históricos* (1841-6), consisting of a general history of medicine (1841-4), a history of surgical operations (1841) and a history of Spanish medicine (1845-6). These works are invaluable for bibliographic reference, worthy successors, in fact, of the *Epidemiologia española* of Joaquin de **Villalba** (1802). The hygienist Luis **Comenge** y Ferrer (1854-) is the author of *Curiosidades médicas* (1886), *Clínica egregia* (1895), medicine in the reign of Alfonso V of Aragon (1903), and notes on the history of Spanish medical culture (1914). Another hygienist, Joaquin **Olmedilla** y Puig has published valuable biographical studies of Andrés Laguna (1887), Nicolas Monardes (1897), Cristobal Acosta (1899) and Vesalius in Madrid (1913). The study of Arnold of Villanova (1879), by Marcelino **Menéndez y Pelayo** (1856-1912), late librarian of the Biblioteca nacional (Madrid) deserves mention here, as also his unfinished history of Spanish science (*La ciencia española*, 1889) and his *Bibliografía hispano-latina clásica* (1902), which represents the work of a lifetime. Apart from the *Bibliotheca* of Nicolas **Antonio** (1672-96), which was reprinted in 1783-88 as a set-off to the *Bibliotheca Lusitana* (1741-59) of Diego Barbosa Machado, the principal bibliographic lists of Spanish literature are the *Diccionario general* of Dionisio Hidalgo (1862-8), B. J. Gallerdo's list of rare and curious books (*Ensayo*, 1863-89), the bibliography of Spanish books of 1401-1833 by Manuel Serrano y Sanz (1903-5), a catalogue of Portuguese authors who wrote in Spanish by Domingo García Perez (1890), a bibliography of Spanish and Portuguese books and translations printed in Italy by Enrico Zaccaria (Carpi, 1907), Mayer Kayserling's list of books by Spanish and Portuguese Jews (Strassburg, 1890), Konrad Haebler's list of Spanish incunabula (1903-17) and Henry Thomas' Short Title Catalogue of Spanish books of 1496-1600 in the British Museum Library (1921). The Junta de iconografía nacional, established in Madrid (1906) for the collection of portraits of national celebrities, has published

an index catalogue of these (*Indice de retratos*) in 10 parts. The respectable tradition for careful bibliography established in Madrid in 1672 has been more than surpassed in the New World. Printing was begun in Mexico in 1539, a century before the Bay State Psalm Book (1640) saw the light, and the first Mexican medical book (1570) antedated Thomas Thacher's broadside on smallpox (Boston, 1677) by 107 years. Mexican literature of the 16th Century has been catalogued in the indispensable *Bibliografía mexicana* of José Garcia **Icazbalceta** (1886-1903), that of the 17th Century by Vicente de **Andrade** (1900), that of the 18th Century by Nicolas **León** (1902-7), the medical historian and anthropologist of Mexico, whose work is based entirely upon original sources in his own country and whose *Adiciones* to Icazbalceta (1903) comprise 116 rare Mexican books printed between 1593 and 1600. In addition, José Mariano Beristain y Souza is author of a bibliography of South American literature by 4000 authors (1883-97) and José **Toribio Medina** has published a history of printing in Mexico during 1539-1821 (1907-9) and special studies of early printing (1904) in Guadalajara (1793-1821), Merida (1813-21), Oaxaca (1720-1820), Puebla de los Angeles (1640-1821) and Vera Cruz (1794-1822). Toribio Medina is, in fact, the leading bibliographer of Latin America. He is the author not only of a bibliography of Spanish American literature of 1493-1810 (1898-1907) but also special histories of printing in Argentina (1892), Chile (1897-99), Bogotá, Colombia (1904), Havana, Cuba (1904), Quito, Ecuador (1904), Guatemala (1910), Paraguay (1892), Lima, Peru (1904-7), Montevideo, Uruguay (1892) and Caracas, Venezuela (1914). Bolivian literature has been catalogued by J. R. Gutierrez (1875-80) and G. R. Moreno (1879-1900), that of Brazil by I. F. Da Silva (1858-1911), A. V. A. S. Blake (1883-1902), and J. C. Rodriguez (1907), that of Chile by Louis Montt (1904-20), that of Colombia by I. Laverde Amaya (1882-95) and Eduardo Posado (1917), that of Cuba by Carlos M. Trelles (1861-1918), that of Ecuador by F. Gozález Suárez (1917), that of Guatemala by J. E. d'Oryan (1917), that of Peru by R. Moreno (1896) and C. A. Pret (1903), that of Uruguay by B. Fernández y Medina (1900) and Dardo Estrada (1912), that of Venezuela by Manuel Segundo Sánchez (1910-4). The leading bibliographer of the Philippine Islands was Wenceslao Emilio **Retana**, who catalogued the books (1895-1905) and printers (1908), while Toribio Medina catalogued 420 books printed in Manila during 1593-1810.

To do more than outline the extension of Spanish medicine in the Spanish colonies is beyond the scope of the present survey. Mexico had the first hospital (erected by Cortez, 1524), the first chair of medicine (1578-80), the first medical publications (1570, 1578) and the first medical periodical (*Mercurio volante,* 1772) in this hemisphere. Universities were started at San Domingo (1538), Mexico (1551), Lima (1553, Medical Faculty 1638), Manila (1601,

Santo Tomas 1611) and Caracas (1725), to name only the oldest, but the development of medicine in these Spanish colonies is, for the most part, shrouded in darkness and awaits its historians. Apart from the superlative work of Nicolas **León**, the only investigation of adequate dimensions which has thus far been published is the history of medicine in Uruguay by Rodolfo **Schiaffino** (Montevideo, 1927).

Mention need only be made of the *res gestae* of such men as Eduardo Licéaga (1836-1920), Rafael Lavista, Antonio Peñafiel, Estrada and León in Mexico; of Carlos **Finlay** (mosquito theory, 1881), Juan Guiteras (1853-95), Juan Santos Fernandez (1847-1922) and Aristides Agramonte in Cuba; Gaspar Vianna (kala azar), Oswaldo **Cruz** (1872-1917) and Carlos **Chagas** (*Trypanosoma Cruzi*, 1909), Vital Brazil and Amaral (Instituto Butantan) in Brazil; Carlos Malbran and José Penna in Argentina; or José **Albert** (infantile beri beri 1908-24), T. H. Pardo de Tavera (Filipino materia medica, 1892) and Cristobal Manalang (hookworm, malaria) in the Philippines. Under American government, the public hygiene of the Philippines has advanced apace. An excellent beginning in the medical history of the Philippines was made by Anastasia Villegas in 1923.[28]

The Twentieth Century

In the 20th Century, Spanish medicine made its first noteworthy contribution to the broad current of European medicine in the work of Santiago **Ramón y Cajal** (1852-) and his pupils.

The son of an Aragonese surgeon, Cajal had in his composition the hardy independence, self-will, tenacity of purpose and long memory of the man of mountaineer stock. Having damaged his health from tropical infections during service as a medical officer of the Spanish Army in Cuba (1874-5), he held in succession the chairs of anatomy at Zaragoza (1877), Valencia (1884) and Barcelona (1887), where he got such results in neurohistology from his modification of the silver-chrome stain invented by Golgi (1880-85) that his appointment to the Madrid chair, coincident with the publication of his great memoir on the retina (1892), was a foregone conclusion. With the aid of his silver nitrate-pyrogallic acid stain (1903), his gold-sublimate stain (1913) and other methods devised by him, he elucidated the finer anatomy of the entire nervous system as never before, and with a single eye to the ultimate rôle of these minutiæ in the dynamics of nervous function. He founded the *Revista trimestral micrográphica* (1897), was ap-

[28] A. Villegas: *Ann. Med. Hist.*, N. Y., 1923, V, 229-241.

pointed director of the *Instituto nacional de higiene de Alfonso XIII* (founded 1900) and in 1903, acquired a Laboratio de investigaciones biologicas (Madrid), which after his retirement, became the Instituto Cajal. He was awarded the Moscow prize of the International Medical Congress at Paris (1900), the Helmholtz medal of the Royal Prussian Academy (1904) and, in 1906, the Nobel Prize, conjointly with Golgi. In 1913-14, Cajal summarized his lifetime of labor in his great treatise on Degeneration and Regeneration of the Nervous System, printed at the expense of Spanish physicians in Argentina and reissued, fifteen years later, in English translation by the Oxford University Press (1928). This deals, as stated, with the minute structural basis of neurodynamics (*anatomia animata*) and its rôle in the transmission of nervous impulses, localization of function, degeneration and regeneration of the neurons and axons of the nerve centers.

In his youth, Cajal had cherished the audacious dream of founding a school of Spanish histologists and he succeeded in a measure probably far beyond his expectations, comparable, indeed, with that of Pavlov in Leningrad. Memorable among the pupils of Cajal are

Nicolas **Achúcarro**, (1851-1918), who devised a stain for connective tissues and worked mainly on the neuroglia; Pio del Rio **Hortega**, who discovered the microglia and oligodendria cells (1919); Francisco **Telló**, who succeeded to Cajal's chair of histology in the Madrid Faculty and has worked on the neurofibrillæ, transplantations of cerebral nerves and regeneration of nerve-endings; Villaverde (neuropathology), de Castro (neuroglia, sympathetic ganglia), Sanchez (comparative neurohistology) and Llorente de Nó (auditory and vestibular nerves).

Finally, Cajal has told the story of his life with straightforward simplicity and charm in his *Recuerdas de mi vida* (1907-17; 2. ed., 1928), while the aphorisms, epigrams and philosophic anecdotes in his *Charlas de café* are among the most pungent and effective to be found in the entire literature of the Latin races. In solid performance, Ramón y Cajal is the greatest figure in the history of Spanish medicine, in point of character, the most eminent man his country has produced in several centuries.

In his autobiography, Cajal laments the "barrier of language" which, in earlier days, stood in the way of a readier acceptance of his work and a similar regret has been voiced by Dr. Eduardo García del Real, professor of history of medicine in the Madrid Faculty, with reference to the gen-

eral ignorance of the outstanding figures of Spanish medicine in Europe and the United States.[29] As the successor of Hernández Morejón and Chinchilla, García del Real has published a history of Spanish medicine (1921),[30] which surpasses any similar record of local medical achievement in any other country. It is a genuine piece of research work, covering nearly 1150 pages, exhaustive, documented, recording with scrupulous fidelity and patriotic devotion every fact and date accessible to its author, with a goodly showing of the cultural achievement of Spain in other branches of science, invention, literature and art.

Yet it is a difficult book to assimilate, partly from lack of a just sense of proportion and literary style and the faulty arrangement of some of the material, but more particularly on account of the lengthy, humorless citations of extravagant eulogy and the apparent failure of the author to strike a balance between what is of definite local importance in Spain and what may be of moment on the broad highway of progressive scientific medicine. With this criterion in mind, he could have said all he has to say in a fraction of the space required, and he might have coördinated his facts and dates to better purpose by stripping down the lengthy eulogies to their bare essentials. The barrier of language, then, lies not in the Spanish idiom itself, which is beautiful, graceful and easy of comprehension, but in the fact that where Spanish poetry is often concise and to the point, Spanish prose, and particularly Spanish scientific prose, is too prone to be diffuse, verbose, florid and rhetorical. The Spanish language is, in fact, a social and artistic, rather than a scientific medium. Yet the spoken idiom, the *chistes* and *coplas,* the national proverbs, the dialogue in Tirso de Molina, the epigrams in

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[29]One necessary and sufficient reason for this spirit of *nil admirari* in the past was the antipathy created among the Northern (Protestant) nations by the Counter-Reformation (Thirty Years War), the Great Armada and the invasion of the Netherlands. The irritation of the people of the Italian principalities against the Spanish viceroys, superimposed by Isabel Farnese, is a leading motive in Stendhal's novel, *La Chartreuse de Parme.*

[30]E. García del Real: *Historia de la Medicina en España,* Madrid, 1921.

the *Charlas* of Cajal are as terse and to the point as the rollicking Gammer Gurton verses of the Arcipreste de Hita or the *Humoradas* of Campoamor, in which not a syllable is wasted. A fair example of the concision of which Spanish poetry is capable is afforded in the sonnet of Castelo y Serra in memory of Argumosa, the most eminent Spanish surgeon in the first half of the 19th Century:

"Grave, severo, mesurado, frio;
Buen esposo, buen padre y ciudadano;
Por su carácter, todo un espartano;
De trato dulce, aunque exterior sombrío.
Como Catón incorruptible, pío;
Correcto en la diccíon, firme de mano;
Como muy pocos, habil cirujano;
A la hora del deber nunca tardío.
Tan pulcro en el obrar como en el traje,
Y docto en escribir castiza prosa
Como en poner artístico vendaje
Despues de hacer operación pasmosa,
Y genio, en fin, de superior linaje,
Tal fué, señores, Diego de Argumosa."

Sophisticates of our flippant post-bellum period may smile at the measured, sober-sided, pedestrian eulogy of these verses, even as pudibond readers of the Victorian "Age of Innocence" would experience horripilation at the sexual cynicism of present day poetry and illustration. Yet judged by the standards of the time in which it was written, the above sonnet is no more lapidary than scores of others of the same period, from Wordsworth or Shelley to Lowell or Swinburne. What it does say to us is that for Spain, too, is apposite the dictum which Mr. Matthew Arnold applied to the literature of our own country: "The glorification of the average man is too much of a religion there." The best one can say of many of the Spanish medical authors cited by García del Real is that they wrote books of average merit on the subjects and specialties in which they happened to be interested. The Fifth Paragraph of Army Regulations, which forbids, "the foolish face of praise" as well as blame, holds up a value seldom appreciated by the historians of science and medicine. The

victim of maladroit laudation by benevolent big-boy enthusiasts at festal dinners and banquets may live to regret the sensible sobriety of more spacious days—

"Ni cet excès d'honneur, ni cette indignité";

or even the acid tests of a more ironic and aristocratic period—

"Go on, dear creatures, make me see
All that disgraced my betters meet in me,"

or

"Is this a dinner? This a genial room?
No, 'tis a temple and a hecatomb,"

or

"I sought no homage from the race that write,
But hid like Asian monarchs from their sight,"

or

"One from all Grub Street doth our fame defend
And (more abusive) calls himself our 'friend'."

The isolation and lack of appreciation of Spanish medicine which García del Real laments is due, in part, to the physical isolation of his country, to the intransigence occasioned by the wars of the Counter-Reformation among Nordics, and to that natural feeling for past glories, which has prevented Spanish historians from evaluating things of merely local consequence with reference to their status (if any) in the larger atmosphere of global medicine. The impersonal scientific contributions of such men as Cajal, Achúcarro, Hortega, Tapía and Barraquer have gone far to lift Spanish medicine out of the same tedious provincialism which once obsessed the medical literature of our own country, and prelude, let us hope, the dawn of a newer and fairer day for Spanish science.

Chronology of Secular and Medical History in Spain

630.	First Greek voyage to Spanish coast.
6th Century.	Scylax refers to Ebro River (Iberus).
550.	Carthaginians enter Spain.
236-228.	Hamilcar Barca enters Spain and founds Barcelona.
219.	Hannibal destroys Saguntum.
206 B.C.-409 A.D.	Roman occupation.
202.	Scipio Africanus defeats Hannibal at Zama (end of Carthaginian dominion).
205 B.C.-14 A.D.	Romanization of Spain.
146 B.C.	Romans destroy Carthage.
A.D.	
306.	First Church Council at Iliberis (Elvira).
409-713.	Visigothic Spain.
554-567.	Athangild establishes Visigothic capital at Toledo.
570-636.	Isidore of Seville.
580.	Bishop Masona founds hospital at Merida.
622.	Conversion of Arabs to Mohammedanism.
711-718.	Moslem conquest of Spain.
711-1031.	Moslem occupation.
732.	Charles Martel defeats Moslems at Tours.
755.	Ommayad capital established at Cordova by Abd-er-Rahman.
755-1031.	Ommayad Dynasty (Cordovan Caliphate).
913-961.	Abd-er-Rahman III (height of Moorish civilization and naval power in Spain).
976-1002.	Almansor.
1031-1276.	Crusade for independence from Moslem rule.
1033.	Monks of Cluny (Benedictines) enter Castile.
1067.	Ruy Diaz (The Cid) founds lazaretto at Palencia.
1085.	Alfonso VI of Castile releases Toledo from Moslem dominion.
1086-91.	Almoravides (Sahara) subjugate Spain.
1086-99.	Ruy Diaz (The Cid) usurps rule of Valencia.
1114-87.	Gerard of Cremona.
1125.	Rise of Almohades in Morocco.
1126-98.	Averroes (Cordova).
1139-1205.	Moses Maimonides (Cordova).
1140.	Archbishop Raimundo founds a school of translators at Toledo.
1146-72.	Almohades subjugate Spain.
1188.	First public assembly (*Cortes*) held in Léon.
1212.	Hospitals at Burgos founded by monks of Cister. Moslems defeated at Navas de Tolosa (Andalusia).
1212-14.	Alfonso VIII founds University of Palencia.
1213-76.	Reign of Jaime I (The Conquerer) in Aragon.
1215.	Alfonso IX founds University of Salamanca. (confirmed 1243; Papal bull 1255).
1230-38.	Establishment of Moslem Kingdom of Granada.
1232-1315.	Ramón Lull.
1236-48.	Ferdinand III of Castile frees Cordova, Murcia and Seville from Moslem domination.
1238.	Jaime I releases Valencia from Moslem dominion.
1240.	Fernando III establishes chair of anatomy at University of Palencia.
1240-1311.	Arnold of Villanova.
1252-84.	Alfonso X ("The Wise").
1252-1479.	Period of development of national unity.
1255.	Alfonso X founds an Academia de Medicina.
1256-65.	Revision of Castilian code of laws (*Partidas*).
1257-73.	Attempt of Alfonso X to become Holy Roman Emperor.
1273.	Rudolph of Hapsburg chosen Holy Roman Emperor.
1282.	Sicilian Vespers. Pedro III of Aragon dispossesses Charles of Anjou in Sicily.
1300.	University of Lerida (reorganized 1575).
1312-50.	Alfonso XI of Castile concentrates royal authority at expense of the nobles.
1322.	Monasterio de Guadalupe (Estremadura) founded, with medical studio and hospital.
1324.	Jaime II of Aragon acquires Sardinia.
1350.	*Amadés de Gaula* circulated in Spain.
1391.	Massacre of Jews in Seville and Barcelona.
1409.	Insane asylum (*Casa de orates*) at Valencia.
1412.	Diego Cobo composes a surgery in rhyme (*Cirugia rimada*).
1422.	Juan II decrees tribunal to examine applicants for right to practice medicine.
1425.	Insane asylum at Zaragoza.
1436.	Insane asylum at Seville.
1450.	University of Barcelona founded.
1458-70.	Catalan revolt.

1468.	Ferdinand of Aragon authorizes dissecting in Hospital de Santa Maria de Gracia (Zaragoza).
1469.	Marriage of Ferdinand (Aragon) and Isabella (Castile).
1471.	Quarantine against plague at Mallorca.
1472.	University of Siguenza founded.
1473.	Insane asylum at Toledo.
1474.	University of Zaragoza founded.
	Printing introduced at Valencia by Lambert Palmart.
1477-8.	Isabella sends 400 ambulances to siege of Otrera.
1479-1516.	Reign of Ferdinand and Isabella.
1481.	Insane admitted to asylum at Barcelona.
1481-1518.	Spanish Inquisition.
1482.	University of Avila founded.
1483.	University of Mallorca founded.
	Hospital de innocentes (insane asylum) founded at Toledo.
1484-9.	Isabella supplies hospital tents at sieges of Alora and Baza.
1490.	Antonio Amiguet founds a school of surgery in Barcelona.
1491-1556.	Loyola.
1492.	Discovery of America. Conquest of Granada. Expulsion of Jews. (March 31).
1494-98.	Julian Gutierrez publishes treatises on stone.
1497.	Ferdinand acquires Naples (Southern Italy).
	Vasco da Gama rounds the Cape of Good Hope.
	Gaspar Torrella describes syphilis as *pudendagra* (abuse of mercurials).
1498.	Villalobos publishes poem on syphilis.
1499.	Pedro Pintor publishes pest-tract.
1500-1665.	Age of Gold.
1500.	University of Valencia founded. (Reorganized 1582).
1502.	Forced conversion of Moors (Mudéjares) to Christianity.
	Juan Almenar discusses treatment of syphilis with mercurials, sarsaparilla, guaiac, sassafras and China root.
1504.	University of Santiago founded.
1504-6.	Reign of Philip the Fair and Juana la Loca.
1506-62.	St. Francis Xavier.
1507.	Heavy epidemic of plague in Spain.
1507-17.	Regency of Ferdinand.
1508.	***Amadés de Gaula*** published at Zaragoza (influence on European fiction).
1512.	Order of Illuminados organized.
1515.	Duke of Ureña founds University of Osuna.
1515-82.	Santa Teresa.
1516.	University of Seville founded.
1516-56.	Reign of Charles I.
1517-1618.	Reformation.
1519.	Charles I of Spain becomes Holy Roman Emperor (Charles V).
1519-21.	Cortez conquers Mexico.
1520.	Charles V founds University of Toledo as Colegio de Santa Catalina.
1521.	Gaspar Torrella publishes *Consilia* on plague epidemic of 1505.
1521-44.	Wars between Charles I (Spain) and Francis I (France).
1525.	Oviedo describes medicinal plants of New World.
1526.	Defeat of Francis I at Pavia.
	Luis Vives publishes treatise on unemployment (*De subventione pauperum*).
1529.	Gutierrez de Godoy publishes brief for breast-feeding of infants.
1531-2.	Pizarro conquers Peru.
1532.	*Constitutio criminalis Carolina* (medical jurisprudence).
1534.	University of Sahagún founded as a *studium generale* (later transferred to Irache).
1534-82.	University of Huesca.
1535.	Andrés Laguna describes the ileocæcal valve.
1537.	University of Granada founded as Colegio de Santa Cruz (1526).
1539-40.	Jesuit order organized.
1540.	Luis Vasseo publishes anatomical tables (4) at Paris.
1540-1606.	Vittoria (sacred music).
1542.	University of Oñate founded.
	Ruiz de Isla publishes book on American origin of syphilis.
1542-52.	Spanish anatomists theorize about the circulation of the blood.
1544.	**Lobera de Avila publishes treatise** on catarrh, gout, stone and syphilis.
1545-1625.	El Greco.
1546.	Charles V authorizes publication of first *Index expurgatorius*.
1547.	Francesco Borgia, Duke of Gandia, founds University of Gandia (Jesuits).
1547-1616.	Cervantes.
1548.	**Andrés Laguna describes method of excising vesicourethral caruncles.**
1549.	Pedro Gimeno describes the stapes in *Dialogus de re medica*.

1550. Montaña de Monserrate publishes *Anatomia* at Valladolid.
1551. Bishop of Osma founds University of Osma as a *studium generale.*
University of Lima (Peru) founded.
Lobera de Avila publishes first Spanish contribution to pediatrics.
1552. Las Casas publishes account of Spanish cruelty to the Indians.
1553. Viceroy of Peru founds University of Oropesa.
University of Almagro founded (Dominicans).
University of Mexico founded.
Servetus describes pulmonary circulation.
1556. Valverde de Hamusco publishes treatise on artistic anatomy.
1556-98. Philip II.
1557. **Typhus fever (*tabardillo*) appears in Spain.**
Juan Huarte completes treatise on vocational aptitude (*Examen de ingenios*), published in 1580.
1558. **Charles V renounces crown of Holy Roman Empire.**
1562-1635. **Lope de Vega.**
1564. **Francisco de la Reina adumbrates circulation of the blood.**
1565. University of Baeza founded.
Porcel described the plague of Saragossa (1564).
1567-1604. War against the Netherlands.
1568. Archbishop of Valencia founds University of Orihuela (Dominicans).
1569-71. Nicolas Monardes publishes accounts of West Indian materia medica.
1570. **Francisco Bravo describes *tabardillo* (Mexican typhus).**
Epidemic of sweating sickness in Spain.
1571. Philip II wins naval victory at Lepanto.
Castillian Cortes requires degree of bachelor of astrology as essential to medical degree.
1571-1658. Tirso de Molina.
1572. Archbishop of Tarragona founds University of Tarragona.
1574. Torrella and Toro describe Spanish typhus (*tabardillo*).
Amatus Lusitanus describes valves of azygos vein.
1576. Francisco Arceo publishes book on wound treatment.
1580. Heavy epidemic of influenza in Madrid and Barcelona.
1580-81. Annexation of Portugal.
1583. University of Gerona.
Diphtheria (*garrotillo*) epidemic in Spain.
1584. 6778 students at the University of Salamanca.
1584-5. Luis de Lemos publishes commentary on Hippocratic writings.
1585-6. Smallpox epidemic in Toledo.
1587. Drake burns shipping in the harbor of Cadiz.
Trial and execution of Mary Stuart.
1588. Defeat and wreck of Invincible Armada.
Philip II establishes prescriptive rights of protomedicate.
1589. Arceó's book on wound-treatment (1576) translated into English.
1590. Gómez Mendez, Bishop of Albarracin, publishes book on massage.
1591. Acosta describes Andes mountain sickness.
1595. Luis Mercado publishes book on visceral diseases.
1596. Lopez de Hinojoso publishes surgical treatise in Mexico.
1598-1700. Juan Calvo translates Guy de Chauliac into Spanish.
1598-1621. Period of decadence.
1599. Philip III.
1599-1660. University of Vich founded.
1600-1681. Velázquez.
1603. Calderón de la Barca.
Diphtheria epidemic in Spain.
Rodrigo de Castro publishes treatise on diseases of women.
1604. *Don Quixote* (Part I) published.
1605. University of Oviedo founded.
Daza Chacón publishes surgical treatise.
1608. Luis Mercado describes diphtheria (*garrotillo*).
1609. University of Pamplona founded.
1611. Expulsion of Moors.
Cascales publishes pediatric treatise.
Casales, Fontecha and Villareal describe diphtheria.
1613. Luis Mercado publishes treatise on diseases of infants.
1614. Vélez de Arciniega publishes account of animals useful to medicine.
1615. Rodrigo de Castro publishes book on medical ethics.
1617. Second Part of *Don Quixote* published.
University of Solsona.
Philip III orders reexamination of provincial physicians coming into Madrid (November 7).
1618-48. Thirty Years' War.
1618-82. Murillo.
1619. 32 Universities in Spain.
1620. Bonet publishes book on training deaf-mutes.
1622-42. Cardinal Richelieu.

1623.	Daça de Valdes publishes first account of spectacles.
1624.	Philip IV creates Estudios de San Isidro.
1629.	Zacutus Lusitanus publishes book on history of medicine.
1635-59.	War with France.
1637-68.	Revolt and independence of Portugal.
1638.	Zacutus Lusitanus publishes treatise on eye diseases.
	Countess of Chinchon (Peru) cured of malarial fever by quinine.
1639.	Quinine imported into Europe by Juan Lopez de Vega.
1640-59.	Catalan Revolt.
1642.	Pedro Barba describes medicinal virtues of quinine in *Vera praxis.*
1643.	Condé defeats Spanish infantry at Rocroy.
	Dismissal of Olivares.
1643-1715.	Louis XIV (*Il n'y a pas de Pyrenées*).
1645.	University of Tortosa founded.
1647.	Epidemic of plague in Valencia.
1649.	Epidemic of plague in Seville.
1650.	2061 students at the University of Alcalá.
1651-60.	Velázquez depicts dwarfism and idiocy by oil-painting.
1659.	Pyrenees made boundary line between France and Spain.
	Marriage of daughter of Philip IV (María Teresa) with Louis XIV.
1665-1700.	Charles II.
1667-97.	Intermittent warfare with European powers.
1672.	Nicolas Antonio publishes *Biblioteca hispaña nova.*
1681.	Botanic Garden in Barcelona.
1685.	Calderon publishes treatise on criminal jurisprudence.
1696.	Nicolas Antonio publishes *Biblioteca hispaña vetus.*
1697.	University of Mallorca refounded.
	Limón Montero publishes first account of Spanish mineral waters.
1699-1776.	Pedro Virgili.
1700.	Real Academia de medicina y cirugia de Seville founded.
1700-46.	Accession of Duke of Anjou as Philip V (Bourbon line).
1701-14.	War of the Spanish Succession.
1702-48.	Wars with England.
1713.	Real Academia Española founded.
1713-14.	Loss of Spanish possessions in Europe.
	Treaties of Utrecht and Rastadt.
1714-48.	Isabel Farnese gains Italian possessions for her children.
1716.	Biblioteca nacional (Madrid) founded.
1717-18.	Philip V reconquers Sicily and Sardinia.
1724.	Abdication of Philip V.
1733.	Real Academia nacional de medicina de Madrid founded.
1734.	*Efemérides barométrico-médicas matritenses* (first Spanish medical periodical) published.
1734-5.	Re-acquisition of Naples.
1740-48.	War of the Austrian Succession.
1743-54.	Financial reforms of Enseñada.
1746-59.	Ferdinand VI.
1746-1828.	Goya.
1748.	Isabel Farnese acquires duchies of Parma, Plasencia and Guastalla.
1751.	Notification of tuberculosis made obligatory (Royal decree of October 6).
1757.	Use of Botanic Garden (Madrid) for instruction.
1759-88.	Charles III (Conflict with England).
1761-2.	Family compact (defensive alliance of Spain with France against England).
1762.	Gaspar Casal describes pellagra.
1762-3.	Temporary occupation of Philippines by the English.
1763.	Real Academia de ciencias y artes (Barcelona) founded.
1764-86.	War with Moslem states on Barbary Coast.
1768.	Gimbernat devises operation for femoral hernia (Gimbernat's ligament).
1771.	Museo nacional de ciencias naturales founded.
1773.	Real Academia de medicina y ciencias (Barcelona) founded.
1774.	Renewal of Family Compact.
1775-83.	American Revolution.
1777-92.	Ministry of Floridablanca.
1779-83.	War with England.
1781.	Botanic Garden in Madrid.
1785.	Biblioteca universitaria (Valencia) founded.
1788-1808.	Charles IV (Conflict with Republican France).
1790.	Bonells and Lacaba publish standard textbook of anatomy.
1792.	Ministry of Aranda.
1792-1808.	Rise of Manuel Godoy.
1795.	Real Colegio de Medicina (Madrid) founded.
1797.	Dismissal of Godoy.
1799.	Education of nurses begun at instance of Gimbernat.
	Anales de historia natural published.
1800.	Francisco Pigillem introduces vaccination into Spain.

1800-1.	Recession of Louisiana to Napoleon. Tuscany added to Duchy of Parma.
1802.	Joaquin Villalba publishes *Epidemiologia española.*
	Trinidad ceded to England.
1803.	Louisiana Purchase.
	Francisco Balmis introduces vaccination throughout Spanish possessions.
1805.	Nelson defeats French and Spanish fleets at Trafalgar.
	Charles IV approves Regulations for the Surgical Corps of the Army (July 20).
1808.	*Dos de Mayo.* Uprising of Spanish people against Napoleon (May 2).
	Abdication of Charles IV (March 19).
1808-14.	Guerilla warfare against Napoleon (Spanish War of Independence).
1808-33.	Ferdinand VII.
1810-24.	Spanish American Colonies gain independence.
1812.	Democratic constitution.
1813.	Wellington defeats the French at Vittoria.
1814.	Ferdinand VII returns to Spain.
1816-17.	Royal orders creating organization (*Cuerpo de Medicos*) of 31 mineral baths.
1819.	Romero performs pericardiotomy.
1821.	Establishment of 23 medical schools in Spain and Colonies.
1823-9.	Terrorist struggle between absolution and insurrection.
1827.	Royal decree uniting medical faculties under a single *Junta* (July 4).
1828.	Protomedicate and Surgeon Generalcy of Army abolished (December 10).
1829.	Ferdinand VII confirms new Regulations of Army Medical Corps (1805).
	Ferdinand VII marries Maria Cristina of Naples.
	Hysera claims priority in operation of blepharoplasty.
1830.	Dr. Mateo Seoane publishes Spanish-American dictionary.
	Regulations of Army Corps of Pharmacists published.
1832.	Royal order limiting personnel of Medical Corps of Navy to 65.
	Argumosa performs parotidectomy, invents syringotome, and claims priority in blepharoplasty.
1832-99.	Emilio Castelar.
1833.	Coronation of Isabel II.
1834.	Hysern publishes treatise on blepharoplasty.
1835.	*Limpieza de sangre* abolished.
	Argumosa performs excision of the tongue.
1837.	New liberal constitution.
1841.	Marcos Viñals describes origin and course of chorda tympani.
1841-6.	Anastasio Chinchilla publishes History of Medicine.
1843.	Pedro Mata publishes plan for reorganizing medical education in Spain (confirmed by Royal Order of October 26).
1843-68.	Reign of Isabella II (Rule of army generals).
1845.	Academia médico-quirúrgica española (Madrid) founded.
	Corral claims priority in vaginal Cæsarean section.
	Toca claims priority in abdominal hysterectomy for uterine tumor.
1845-7.	Mata edits *La Facultad* (medical periodical).
1847.	Real Academia de ciencias exactas (Madrid) founded.
	Diaz activates reforms in popular and medical education.
1847-9.	New plans for reorganization of medical education.
1850.	Special chairs of venereal diseases, dermatology and ophthalmology in Madrid Faculty (Decree of August 28).
1852.	*Historia bibliográfica de la medicina española* (Hernández Morejón) published.
1850-66.	Royal orders modifying plan of 1847 for improvement of medical education.
1854-83.	Mendez Alvaro edits *Siglo médico.*
1855.	Manuel García invents the laryngoscope.
	Law regulating public health (*Ley de sanidad,* November 28).
1856-66.	Marquis del Busto edits *España Médica.*
1857-8.	Marquis del Busto founds and edits *Iberia Médica.*
1857.	Laws reorganizing public instruction (*ley de Moyano,* July 17).
1860.	Rubio y Gali performs first ovariotomy in Spain.
1861.	Reorganization of Real Academia de Medicina (Madrid).
	Rubio y Gali performs hysterectomy.
1868.	New law reforming public education including medicine (*ley de Ruiz Zorrilla,* October 25-27).
1868-78.	Cuban Revolution.
1870.	Assassination of General Prim.
1870-71.	Franco-Prussian War (Claims of Leopold of Hohenzollern to Spanish throne).
1871-3.	Amadeo of Savoy (Duke of Aosta) as temporary ruler.
1871-80.	Olavide publishes treatise on dermatology.
1871-83.	Toro edits *Clinica oftálmologica.*

1873-4.	Temporary Spanish Republic.
1874.	Rubio y Gali performs first nephrectomy in Spain.
1874-85.	Alfonso XII.
1874-1924.	Growth of caciquism (political bosses).
1875.	Museo Antropológico of Dr. Velasco opened (April 29).
1876.	New conservative constitution.
1878.	Academia i Laboratori de ciencias mediques de Catalunya (Barcelona) founded.
	Ribera claims priority over Estlander (1879) for resection of ribs in empyema.
	Rubio y Gali performs laryngectomy.
1879.	Velázquez founds *La Prensa médica de Granada* (*Gaceta médica del Sur de España* 1882).
1880.	Rubio y Gali founds Instituto de terapeutica operatoria (Instituto Rubio).
1881.	Rodriguez Mendez founds *Gaceta médica catalana.*
1882.	Fargas y Roca performs first ovariotomy in Spain for cystic tumor.
1884.	Hernando y Espinosa publishes report on leprosy in Granada.
1885.	Instituto nacional de higiene militar (Madrid) founded.
1885-1902.	Regency of María Cristina.
1888.	Margarit claims priority in interilio-abdominal amputation (Jaboulay, 1894).
1892.	Academia de higiene de Cataluña (Barcelona) founded.
1894.	Llorente y Matos founds Instituto de microbiologia y seroterapia (Instituto Llorente).
1895.	Fargas y Roca performs first gastro-enterostomy in Spain.
1896-7.	Llorente y Matos introduces laryngeal intubation.
1897.	Ramón y Cajal starts *Revista trimestral micrográphica.*
1898.	Spanish-American War. Loss of Cuba, Porto Rico and the Philippines
	Revival of economic prosperity.
	San Martin devises osteoplastic amputation at hip-joint.
	Menéndez y Pelayo becomes director of Biblioteca nacional.
1898-1900.	San Martin experiments on surgical arterio-venous anastomosis.
1898-1931.	Renaissance of Spanish literature, art and music.
1899.	Instituto nacional de higiene de Alfonso XIII (Madrid) founded.
	Ribera devises posterior mediastinotomy.
1902.	Sociedad oftálmologica hispano-Americana (Madrid) founded.
1902-31.	Alfonso XIII.
1903.	First Spanish congress of ophthalmology.
	Cajal founds Laboratorio de investigaciones biologicas (Madrid).
	Ribera describes total gastrectomy.
1903-17.	Konrad Haebler catalogues Spanish incunabula.
1905.	Garcia Tapia describes hemiplegic syndrome allocated to a lesion in the medulla.
	Echegaray wins Nobel prize.
1906.	Ramón y Cajal wins Nobel Prize.
	Barraquer describes progressive lipodystrophy.
1908.	Asociación española para el progreso de las ciencias founded.
1909.	Catalonian revolt. Execution of Ferrer.
1910.	First Spanish Congress of Tuberculosis at Saragossa.
1912.	General railway strike. Canalejas invokes martial law.
1913.	Sociedad de biologia (Barcelona) founded.
1913-14.	Cajal publishes treatise on Degeneration and Regeneration of the Nervous System.
1914-18.	Spain maintains neutrality in World War.
1915.	Sociedad oftalmológica (Madrid) founded.
1917.	Barraquer devises method of extracting cataract (phakoeresis).
1919.	Rio Hortega investigates microglia and oligodendria cells.
1921.	Sociedad española de antropologia founded.
1923.	Instituto Alfonso XIII for cancer research (Madrid) founded.
1924.	Liga español contre el cancer (Madrid) organized.
1925.	Sociedad oftalmológica de Barcelona founded.
1931.	Revolution. Organization of Spanish Republic.

FIELDING H. GARRISON.

CANCER AS A COMPLICATION OF SKIN DISEASES

(Lantern Slide Demonstration)

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In this address I shall attempt to give a comprehensive review of the subject of cancer of the skin in its various aspects, and shall corrolate some of my recently published articles.

While the specific cause of cancer is yet unknown, it is now pretty well agreed that repeated irritation and other inflammatory processes in the tissues play a rôle in the excitation of cancerous growths. This is exemplified particularly well in the field of dermatology. Most malignant new growths of the skin, mouth, and external genitalia are preceded by some previous injury or skin condition such as keratoses, syphilis, X-ray burns, tuberculosis of the skin, sebaceous cysts, etc., and there are about twenty skin conditions known to be precursors of such growths. The dermatologist has an opportunity to obtain satisfactory results in the majority of his cases of malignant lesions for the apparent reason that they are of the accessible type in his field. Not only is there opportunity for the growth to be seen early, but correct diagnosis may be made readily by microscopic studies of sections of tissue which can be taken with facility. The importance of taking biopsies for microscopic examination cannot be over-emphasized, especially

so in the differential diagnosis of the indurative and ulcerative lesions, i.e., syphilis, tuberculosis, granuloma inguinale and ulcerating carcinomas. The information often to be gained by histologic study warrants the taking of a biopsy. With the exception of melanomas the removal of a small selected portion of accessible tissue seldom results in any harm. The section should always be taken from the edge of the lesion including a small part of the apparently normal appearing tissue, for if the section is taken from the center of the ulcerating lesion it may show nothing more than granulation tissue. If the diagnosis is made microscopically there will be avoided the all too frequent mistake of treating a patient for syphilis because he had an ulcerating lesion coincidental with a positive blood test; the doctor, therefore, overlooking the fact that the lesion was a cancer in a patient who had systemic syphilis. Also the degree of malignancy and its radiosensitivity may be determined in the case of a neoplasm.

The majority of new growths of the skin if thoroughly treated, result very satisfactorily. The prognosis in this field of work is generally much more favorable than any other, and especially in early cases a very high percentage remain well permanently. If in addition, the general practitioner would learn to recognize those skin conditions which are forerunners of cancer and also to advise patients to eliminate all irritative factors, such as chronic ulcerations, keratoses, over-smoking, ill-fitting dentures, poor oral hygiene, he would be doing important work in the prophylaxis of malignancy. Such organizations as The American Association for Cancer Research and The American Society for the Control of Cancer have helped considerably along the lines of prophylaxis against this disease, and most workers in the field of malignancy are now seeing a large number of their cases much earlier in their course of development than previously. The importance of this work is easily demonstrated by the fact that the results are infinitely more satisfactory when the tumor is treated while yet localized and before metastases have occurred in the adjacent lymphnodes or in other parts of the body.

Leukoplakia of the Mouth

Leukoplakia of the mucous membranes of the tongue and buccal mucosa has always been regarded as being potentially dangerous, because it has so frequently been followed by cancer, especially in advanced cases.

Cancer supervention in leukoplakia of the mucous membranes of the mouth, and especially of the tongue, has been reported so frequently, that the laity and even the medical profession have been inclined of late to exaggerate the production of cancer in leukoplakic patches. It should be understood that the greater number of cases of leukoplakia do not eventuate in cancer, especially when all forms of irritation are removed. Large numbers of people have leukoplakia of the mouth for many years without subjective symptoms and with no signs of malignancy. This does not mean, however, that the leukoplakia is not potentially malignant, for when these white patches begin to fissure or to show signs of inflammation they are either beginning to be malignant or are actually cancerous. Bloodgood considers leukoplakia second in importance to bad teeth in the etiology of cancer of the mouth. In a series of 160 cases of cancer of the tongue in men he found leukoplakia in 25 per cent of their number; Mantilla, in studying 566 cases of leukoplakia, reported in the literature by various writers, found that in 32 per cent cancer had resulted. However, for the general run of cases of leukoplakia of the buccal mucosa this percentage seems rather high. Most observers agree that leukoplakia of the tongue and lips is far more prone to become cancerous than leukoplakia of the buccal mucosa and gums. Repeated irritation may result in leukoplakia alone, or in cancer alone, or a combination of both.

Etiology.—While much has been written on the causes of leukoplakia of the mouth, there has been great diversity of opinion, especially as to the rôle played by syphilis.

Sex.—Leukoplakia shows a striking predilection for the male sex. In Fox's series of 40 cases there were 38 men

and 2 women. Cumston in a collection of over 800 cases in the literature, including 10 of his own, found only 30 females with this condition.

Age.—DeForest considers leukoplakia to be most frequent in the fifth and sixth decades, while Eichenlaub's group of 70 cases ranged in age from 28 to 55 years, averaging about 32. Fox's average was 48.

Syphilis.—Much has been written to show that syphilis has preceded leukoplakia in a large proportion of cases. Fournier reported that 80 per cent of his patients with leukoplakia had previously been infected with syphilis. His group consisted of 324 patients. In 65 per cent of Fox's cases a previous syphilitic infection was judged to have occurred from the history, Wassermann reaction, or presence of tertiary manifestations. Highman states that "leukoplakia buccalis is almost invariably syphilitic," while Pusey is of the opinion that long-continued irritation will produce leukoplakia, and is not inclined to believe that the association with syphilis is of great significance. Hazen and Eichenlaub conclude that "syphilis represents an accidental rather than a causative factor in this disease." Later Eichenlaub, in reporting an additional series of 70 cases of leukoplakia observed among 349 patients examined by him, found that 3.2 per cent of the entire group had syphilis while 17 per cent of the leukoplakia group had syphilis. Eichenlaub's report gives one the impression that he does not believe syphilis plays an important rôle in the causation of leukoplakia.

Elliott and Stookey in a study of the oral mucosa of 50 patients with neurosyphilis found 49 patients with definite leukoplakic patches.

Tobacco.—There appears to be a general agreement among the various writers that users of tobacco, especially smokers, are the patients who are most prone to leukoplakia. Butlin forty-five years ago stressed the importance of smoking as one of the important causes of leukoplakia. Since then other writers have supported his ideas. Of

Fox's 40 cases, 35 were habitual smokers. Max Joseph considers that the "severity of leukoplakia depends upon the greater or less use of tobacco." Perhaps the reason that this condition is observed so much more frequently in men is because the latter are much greater users of tobacco.

Teeth.—Hazen and Eichenlaub emphasize the fact that "rough teeth by causing mechanical irritation inaugurate the disease in the vast majority of cases." Bloodgood also notes the frequent association of bad teeth with leukoplakia.

Alcohol and Food.—Various writers mention that strong alcoholic beverages and highly seasoned foods are probably an exciting cause of leukoplakia in some cases.

Gastro-Intestinal Disturbances.—Montgomery is of the opinion that "the chief cause of leukoplakia is syphilis, next tobacco, and finally a chronic catarrhal and therefore irritable state of the mucous membranes usually found in connection with chronic fermentative intoxications along the alimentary tract."

I have observed a patient in private practice, the wife of a dentist, who has repeatedly had patches of leukoplakia on the tongue and buccal mucous membranes. The appearance of these patches gave no symptoms and the possibility of a drug eruption was excluded. When the patient was first examined two years ago this history was given us by her husband. Since then we have been able to confirm his observation that the patches disappeared without any local treatment during the time when the patient's digestive system was apparently functioning normally.

Comment on etiology (race and occupation).—There is no doubt that syphilis precedes leukoplakia often enough to be considered an important predisposing factor. However, it should be fully understood that *leukoplakia is in itself not a syphilitic process,* for microscopically this condition does not give the picture of syphilis, but has the same structure as leukoplakia in non-syphilitic patients. Also it has been

definitely observed that the condition does not improve under anti-syphilitic treatment, whether associated with syphilis or not.

I believe that whether or not the patient has had a previous syphilis (excluding active syphilis), some form of local irritation is usually the exciting cause of leukoplakia, the most important irritant being tobacco. This year I have had two patients who presented slightly infiltrated extensive white patches on the tongue and buccal mucosa, one with a history of seven years', the other two years' duration, both of whom had been heavy smokers over a period of years. By discontinuing all forms of tobacco and with the use of a mouth-wash of ordinary milk of magnesia, the leukoplakia in both of these patients had almost entirely disappeared. There were no evidences of syphilis and the teeth were in good condition.

While leukoplakia buccalis may also be caused by other irritants such as necrotic or jagged teeth, alcohol, the chewing of betel-nuts among Orientals, very hot or highly spiced food and gastro-intestinal disturbances, I agree with the majority of the writers who consider that syphilis and tobacco are the most important etiological factors, and that where syphilis had existed or does exist, smoking should be reduced or prohibited.

Treatment.—In the treatment of leukoplakia buccalis prophylaxis is the all-important factor. The prevention or removal of all possible irritants such as those mentioned here in the discussion of the etiology is advisable. Anti-syphilitic treatment in syphilitic patients suffering from leukoplakia benefits the true syphilitic condition but fails to cause a disappearance of the leukoplakia. It may, however, make the tissues less susceptible to the development of cancer.

In reference to the removal of irritants it must be borne in mind that the vast majority of people who subject their oral mucosa to irritation by smoking, alcohol, spicy foods, very hot and very cold foods, etc., do not present leuko-

plakia. Direct injuries must be avoided as from jagged or necrotic teeth, improper dentistry, biting of the tongue or mucous membranes, the use of hot clay pipes on the lips or tongue, and outright inveterate smoking. There are certain persons whose mucous membranes are more sensitive than those of the average, just as there are some who are more prone to eczematous eruptions of the skin than others. In patients with an apparently more sensitive mucous membrane, abstinence from all forms of irritants and the avoidance of gastro-intestinal disturbances is advisable.

For the ordinary mild case of leukoplakia discontinuance of all irritants, with a bland mouth-wash, is sufficient for improvement. The condition, however, recurs promptly when these measures are not followed. Where the patches are more resistant and show the slightest tendency to proliferate or to fissure, they should be promptly destroyed by means of electrocoagulation. Where the leukoplakia is less infiltrated and removal is desired, electrodesiccation is the treatment of choice. While leukoplakia may recur under this treatment, it is less likely to do so if strict attention is paid to avoidance of irritants.

I shall mention the following therapeutic agents only to condemn them; radium, roentgen rays, carbon dioxide snow, chemical caustics of all kinds, and electrolysis.

Syphilis

The leukoplakia which occurs on the mucous membranes of the mouth, tongue and oral cavity in syphilitic patients has long been recognized as being subject to malignant degeneration. This subject was considered under leukoplakia of the mouth.

Tertiary syphilitic manifestations on the mucosa of the mouth and particularly of the tongue play an important rôle in precipitating carcinomatous growths. A conservative estimate of the numerous recorded cases of cancer of the tongue indicates that this condition is associated

with tertiary syphilis in about 60 per cent of the cases. The syphilitic manifestations may be in the form of gummas, interstitial glossitis, and leukoplakia. The malignant tumors often develop in scars from previous syphilitic ulcerations of the mouth.

The importance of looking upon all infiltrated ulcerations of the mucous membranes of the mouth as being possibly cancerous should be emphasized. Only too often has there been delay in the treatment of mouth carcinomas due to the fact that the patient had serologic evidence of syphilis. Much time may be lost in treating such a patient for his syphilis, while the more serious condition is the cancer, which is so often present instead of the supposedly syphilitic ulceration. Then again there may be a broken-down and ulcerating gumma with cancer supervention. In addition to the time lost in treating the patient for syphilis who has cancer of the mucous membranes there is also another point to be considered. This is the fact that most syphilologists believe that cancerous growths on a syphilitic base are stimulated to more rapid growth by arsenical therapy.

It is considered *imperative that all persistent ulcerations of the mucous membranes be studied microscopically to determine the presence of carcinoma regardless of serologic or other evidences of syphilis.* The tissue to be studied should include the borders of the ulceration, for sections taken from the center of such lesions often show nothing but granulation tissue.

Our only hope at the present time for decreasing the mortality from cancer of the mouth is in its very early recognition, so that therapy may be instituted at once.

The following two cases from our collection illustrate the importance of the above:

CASE 1—J. S.—Male, aged 40 years, was first seen December 31st, 1927. There was present a slightly infiltrated ulceration on the anterior third of the left margin of the tongue. He gave a history of a syphilitic infection twenty

years previously which had been treated by intramuscular injections. The lesion of the tongue was of six months' duration and began as a pea-sized ulcer. The patient then consulted a physician, who after finding a positive Wassermann blood reaction at once instituted anti-syphilitic therapy which was continued for months, during which time the tongue lesion became progressively larger and the patient lost weight rapidly. A section taken from the ulcer for microscopic study showed a prickle-cell cancer on a gummatous base.

Case 2—E. K.—Aged 43 years, appeared with a dime-sized superficial ulceration on the right anterior third of the tongue. This had been present for three months. The blood Wassermann was strongly positive. A biopsy revealed a rapidly infiltrating prickle-cell carcinoma.

Although carcinoma has been observed in both syphilitic ulcers of the glabrous skin and the scars left by them, this incidence is comparatively rare.

Roentgen-Ray and Radium Sequelae

These two agents may produce the same deleterious effects on the tissues. They may do so by one massive overdose or by the accumulation of too great a number of repeated small doses. Sequelæ may not appear for several years following the discontinuation of roentgen-ray or radium therapy. These sequelæ may appear in the following order: pigmentation, telangiectasia, keratoses, ulceration, and in some cases cancer. An ulceration can occur within a few months after a single large overdose of roentgen rays, and cancer may soon develop in such ulcers. The prickle-cell cancer is the type invariably found, and as a rule begins on a keratosis.

Treatment.—It is recommended that radical surgical excision be instituted as early as possible when ulcerations appear as the result of roentgen rays or radium. All radium and roentgen-ray keratoses should be destroyed by some form of high-frequency current such as electro-

coagulation. We cannot see the rationale of treating roentgen-ray and radium sequelæ with the same agents which have produced them. Although such therapy is commonly used, I feel that it is strongly contra-indicated.

Moles.

Although any mole may be the site of malignant change, usually only certain clinical types are apt to develop into melano-carcinomas. This type is the bluish-black or slate-black mole, which as a rule is non-hairy. It may be flat or slightly raised. When flat and level with the surface of the skin it has been called "malignant lentigo." In the mole, which is a potential melano-carcinoma, both the pigmented and non-pigmented nævus cells are of ecto-dermal origin. This type of cancer often rapidly metastasizes, and the disseminated tumors, while usually pigmented, may be without pigment.

Although Dawson and others doubt the existence of true melano-sarcomas, they have been reported as arising from moles where the nævus cells were located in the cutis and without apparent derivation from the epidermis—nævus cerebelliformis; blue nævus (Bloch).

However, most moles are essentially benign. A proof of this is that practically every person has one or more moles, the vast majority of which never give rise to cancerous growths. The moles which are not inclined to malignancy may be conveniently classified clinically as follows:

1. Non-pigmented moles:
   a. Fibroma molle.
   b. Fibroma durum.
2. Pigmented moles of benign type:
   a. Hairy mole.
   b. Raised brown mole.
   c. Verrucous mole.

The benign mole is distinctly a cutis lesion having no apparent connection with the epidermis.

Treatment.—The benign moles when hairy should have the hairs destroyed by electrolysis. Frequently the mole disappears without further treatment. If not, the remainder may be removed by various methods, their efficacy being in the following order: Carbon dioxide snow, trichloracetic acid and electrodesiccation. Radium and roentgen rays are contra-indicated in the treatment of pigmented nævi. The treatment described for pigmented hairy moles after the hair has been removed by electrolysis applies also to the non-hairy but benign type of mole.

The treatment of the slate-black or blue-black moles requires serious consideration. They are always a potential source of danger, and the prognosis even with the most radical therapy is uncertain. We are of the opinion that if they are located in areas not subject to irritation and if they have not shown signs of growth, it is safer to leave these nævi untreated. Microscopic studies show that the size of the nævus on the surface of the skin may be misleading as to the actual extent in the tissues. I have seen cases where the pigment-bearing cells were found inches away from the small papule on the surface, and where deep down in the fat following along the walls of the blood-vessels and nerve-fibres, pigmented cells could be found on microscopic study. These latter deposits were associated with apparently quiescent moles. When there is an indication for the removal of such nævi, the following procedure should be followed: wide removal by some surgical method preferably the high-frequency knife, followed by electrocoagulation should be instituted before these moles show signs of growth or immediately at their first sign of growth. The excision should be made in the form of a cone the base of which is deep in the underlying tissues. Radium or roentgen rays have been as a rule unsatisfactory when used alone for the treatment of melanomas due to their marked radioresistance and because of the tremendous destructive doses necessary for the removal of these lesions. Irradiation in smaller doses may be useful following the above surgical removal.

Senile Keratoses

Senile keratoses (erroneously called senile keratoma* by some authors) are lesions which occur in individuals usually past sixty years of age, but occasionally are seen in younger people and are located chiefly on the temples, other parts of the face and neck, and back of the hands, i. e., the exposed surfaces. Senile keratoses are most commonly seen in those who are continually exposed to the elements and hence are far more frequently found in men than in women. Senile keratoses are not frequently seen on covered portions of the body. They are flat or slightly elevated, pea to dime-sized lesions, usually multiple, yellowish brown to dark grey or greyish black in color. Their surface is covered with dry, firmly adherent scales or crusts. On palpation they are embedded, sharply marginated, firm and rough. Upon removal of the horny covering with the curette one sees numerous small conical projections on their under surfaces, which had fitted into the depressions (dilated follicular orifices) which are thus disclosed. When the crust is removed, the surface exposed is moist and red, often slightly hemorrhagic and superficial ulceration may occasionally be present. In the uncomplicated case of senile keratosis there are as a rule no subjective sensations and generally there is no clinical evidence of inflammatory reaction. Usually these lesions are accompanied by other evidences of senile changes in the neighboring skin, e. g., dryness, freckling, hyperpigmentation, telangiectasia and wrinkling. The clinical diagnosis of the lesions on the back of the hands presents no difficulty. This however is not the case with the face lesions, some of which might look identical with seborrheic keratoses, particularly in patients of advanced years. Two of our face lesions which had been clinically diagnosed senile keratoses proved to be seborrheic keratoses microscopically.

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*Keratoma—strictly speaking meaning a tumor of the horny layer and applicable only to a cutaneous horn.

The histologic findings in uncomplicated cases of senile keratoses are fairly uniform and present a definite microscopic picture.

Seborrheic Keratoses

Seborrheic keratoses* are found on the chest, interscapular region, about the waistline and on the face. The chin and submental regions are rarely involved. I have never seen a seborrheic keratosis on the back of the hands. These lesions are practically always multiple and may vary from three or four to one hundred or more. They are sharply circumscribed, rounded or oval, flat elevations varying in size from a pea to a silver quarter. As a rule they are covered with greasy friable scales and are grey, yellow, brown or black in color. They present a granular surface which is raised one to three mm. above the level of the skin, and usually the whole lesion is freely movable over the underlying skin; this explains why they are so readily removed with the curette. On removal one finds a small, wart-like projection in the center of the underlying skin. Often small black points or dots are present on the smooth elevated surfaces; these correspond to the follicular openings. Uncomplicated cases do not present clinical inflammatory reaction. Whatever the etiology of seborrheic keratosis is, I agree with MacLeod, Sutton, Pusey and Unna, and others who believe that they bear some relationship to and are found most often in association with a greasy seborrheic skin. They are characteristically slow in evolution, do not tend to disappear spontaneously, and are seen as a rule in individuals past forty years of age, e. g., they occur more often in a younger group of individuals than do senile keratoses.

Subjective symptoms are usually absent, although there may be itching or a sense of irritation at times.

*Synonyms occasionally used are verruca senilis vel plana, verruca seborrheica, keratosis pigmentosa, nævi seborrheica (Unna), acanthosis verrucosus seborrheica (Walch), senile verruca (Freudenthal).

When seborrheic keratoses involve the face it is sometimes impossible to differentiate them clinically from the lesions of senile keratoses, especially in those lesions that take on a warty appearance and are covered with tightly adherent scales.

Seborrheic and Senile Keratoses
Susceptibility to Malignant Change.

These two conditions should be separated because they vary in importance as regards their relationship to malignancy.

The clinical course of senile keratosis varies. The lesions do not disappear spontaneously, and may persist unchanged for months and even years. Hazen estimates that about 5 per cent of them undergo epitheliomatous transformation. They either ulcerate superficially or the lesion enlarges gradually and becomes elevated with a marked hyperkeratotic covering. At times they may assume a papillomatous appearance. When such changes occur the growth is undoubtedly undergoing epitheliomatous development if it is not already a prickle-cell epithelioma. The appearance of an inflammatory border about a senile keratosis which has recently shown a tendency to enlarge, is one of the first clinical signs of malignancy. Also when a senile keratosis becomes verrucous, it is a carcinoma. The type of senile keratosis which has a tendency to become verrucous has been called the acanthoid or verrucous type of seborrheic keratosis by Sutton. Senile keratoses therefore are extremely important precancerous lesions. Their histopathology, is such that when and if a carcinoma results it is always of the prickle-cell variety. The fact that seborrheic keratoses rarely if ever occur on the back of the hands (I have never observed one), while such a location is the favorite site of senile keratoses, would seem to explain the clinical finding that the vast majority of all cancerous lesions of the hands are prickle-cell epitheliomas.

Seborrheic keratoses of the face not uncommonly give rise to epitheliomas. On the basis of the histologic find-

ings, when such a malignant change does occur, the resulting epithelioma is of the *basal-cell variety.*

Resume

(1) Senile keratoses and seborrheic keratoses are two distinct disease entities clinically and pathologically. A clinical differentiation is not always possible when these two conditions occur simultaneously on the face.

(2) Senile keratosis is distinctly a precancerous condition. While such lesions may exist for many years without undergoing malignant changes or may never undergo such a change, yet if it does occur the epithelioma is always of the *prickle-cell type.*

(3) Senile keratoses may occur on other than exposed portions of the body and recently I have seen two instances, one of which was on the penis.

(4) Seborrheic keratosis may develop into an epithelioma. When it does, it is usually on the face and is always of the *basal-cell variety.*

Kraurosis Vulvae

Briesky in 1885 in an epochal contribution gave the name "kraurosis" to the following syndrome: Retraction of the tissues of the female external genitalia (kraurosis) with whitening of the integument (leukoplakia). In greater detail these changes consisted of an atrophic and sclerosed condition of the skin of the vestibule and the labia minora, together with the frenulum and prepuce. The skin in areas where retraction was most pronounced was white, dry and covered in places with a thick and toughened epidermis. The adjacent skin was of a dry, glazed, washed-out, whitish appearance (leukoplakia). Since that time there have been various contributions to the literature on this subject. Some authors regard kraurosis and leukoplakia as two distinct and unrelated diseases (Jayle and Bender, Thibierge, Berkeley and Bonney); others believe kraurosis and leukoplakia to be dif-

ferent manifestations of an identical pathological process. Graves and Smith, in a most thorough and recent review of the subject, presented clinical and histological evidence that "kraurosis and leukoplakia used in the classic sense are phases of an identical process."

Kraurosis vulvae, in its classical sense, has been regarded since its recognition as a precursor of cancer. Jayle says "leukoplasic kraurosis is complicated with cancer in about one-tenth of the published cases." Smith, who made a histological study of 21 specimens of vulvar cancer, found leukoplakia 16 times and kraurosis 14 times. He felt that his studies "proved sufficiently well that cancer of the vulva is at least in the majority of cases preceded by leuko-kraurotic changes."

Treatment.—When permanent skin changes of a leukoplakic nature are present it is useless to temporize with various local applications for the condition requires surgical treatment. A partial or complete vulvectomy should be done followed by the plastic work necessary for good genital drainage. Such surgical therapy in most cases gives permanent relief from symptoms and is a preventative against future cancer. Roentgen-ray and radium therapy not only is useless but contra-indicated in the treatment of kraurosis vulvae.

Lupus Vulgaris

Lupus vulgaris as a precursor of cancer was reported in the literature by Hutchinson, Bayha, Hebra, Kaposi and others over forty years ago, and therefore before the discovery of roentgen rays and radium. Numerous investigators have contributed reports of lupus vulgaris carcinoma. There has been much controversy concerning its increase as a result of the use of roentgen rays and radium in the treatment of lupus vulgaris. Some observers are of the opinion that doses of roentgen rays well within safe limits, as we understand them, may precipitate cancerous growths in this disease. Others feel that roentgen rays or radium will cause cancer in lupus vulgaris only

as a result of definite overdoses given either massively or fractionally. In other words, the latter class of cases would belong to the group of roentgen-ray and radium carcinomas.

Lupus cancer most often begins in a lupus lesion or scar of many years' duration. When once started the cancerous growth is rapid, and although the prickle-cell carcinoma is the usual type met with, metastases are not frequent. Hutchinson did not note gland metastases in his 12 cases. Walker, fourteen years later, remarked that metastases were exceptional. Vilanova, however, recently reported a case in which there were fatal metastases. Pautrier's case of lupus vulgaris was interesting because of the occurrence of multiple foci of basal-cell epithelioma in a lupus patch.

Lupus vulgaris cancer is not simply a cancer of scar tissue in the same sense as one appearing on the scar of a burn, for here the process is a very slow one, while lupus vulgaris cancer is usually acutely destructive locally. Hutchinson, who believed this, has numerous supporters. Although Gaucher and Stumpke have blamed roentgen rays as a cause of epitheliomatous growths developing on lupus vulgaris, I am in accord with Louste and MacKee that the technique of radiotherapy rather than the agent is to be blamed. Lieberthal, Zeisler, Pusey, Anthony, Hyde and Ambrossoli have all reported cases of epithelioma on lupus vulgaris in which roentgen rays or radium had not been used.

Norman Walker reported that 31 per cent of his cases were under forty years of age. In describing the cancer of lupus vulgaris he remarked that it was often papillomatous and unaccompanied by hyperkeratoses, which latter are found in roentgen-ray cancer.

Leloir estimated the frequency of cancer as about 2 per cent in lupus vulgaris cases. Du Bois Havenith found 5 cases of carcinoma in 118 cases of lupus vulgaris. This percentage is probably high, although Ormsby estimated

that cancer occurs in from 2 to 4 per cent of the cases; and Darier and Pollitzer place its frequency at 4 per cent.

Wild noticed that lupus vulgaris cancer was of two clinical types: first, the fungating type which spreads rapidly and forms a growth of considerable size, and the second which breaks down with deep ulcerations. Sequeira found prickle-cell growths in 13 out of 14 cases of lupus vulgaris cancer.

Summary

(1) The incidence of cancer in lupus vulgaris varies between 1.5 and 4 per cent.

(2) Prickle-cell carcinoma is the type usually found.

(3) The face lesions of lupus vulgaris are those most likely to become malignant.

(4) The development of epithelioma is more frequent in the male, although lupus vulgaris is more common in the female.

(5) While carcinoma usually occurs in cases of long-standing lupus vulgaris, this complication is seen rather frequently in patients under forty years of age.

(6) I believe that the number of cases of lupus vulgaris cancer has been increased by the use of roentgen rays and radium, *but only as a result of over-dosage.*

(7) Metastases have been comparatively infrequent. This might be explained on the basis that the cancer is growing in an already fibrotic and scarred tissue in which the lymphatics have been practically obliterated.

Occupational Keratodermas

There have been numerous reports of cancer of the skin due to occupational exposure to various chemicals. These malignant growths, which usually are of the prickle-cell type, are invariably preceded by keratoses. What percentage of workers in industries develop keratoses and

what percentage of these develop cancer cannot be judged from the reports in the literature or from available statistics.

O'Donovan, who has reviewed this subject, considers "tar carcinoma" to be the most frequent occupational cancer in England. Tar contact may occur in the following occupations: tar distillers, gas-works stokers, creosote workers, tar road sprayers, chimney sweepers, paraffin workers, benzine distillers, anthracene labourers, coal oil workers, pitch handlers, lamp-black workers, aniline dye workers and sprinklers of soot (gardeners).

"Arsenical cancer" of occupational origin: In this group are included sheep-dip workers who come in contact with much arsenic dust. Arsenical keratoderma and cancer may also occur in workers with Paris green (rat poison), wall-paper makers, smelters of ores, such as tin, nickel, lead, copper, iron, and silver, furriers, tanners, farmers using arsenic sprays and in taxidermists.

Other workers in which keratoses and resulting cancers occur are handlers of heavy grade mineral oils, shale oil workers, mule spinners (scrotal cancer), brewers, and workers with roentgen rays and radium. Here also may be mentioned that cancer has been frequently reported in Tibetans, who are in the habit of wearing little hot "stoves" against their abdomens in cold weather.

Arsenical Keratoses

Here will be considered only the keratoses resulting from the internal use of arsenic. Hutchinson, as far back as 1887, recognized the possibility of cutaneous cancer following keratoses due to the long-continued internal use of arsenic and reported several such cases.

Some 60 cases or more of cancer following arsenical keratoses are present in the literature. In most instances the squamous-cell type of cancer was noted.

Practically all observers agree that epithelioma may follow cutaneous hyperkeratoses which are the result of

arsenic taken internally. What rôle does the arsenic play in the production of cancer and what is the modus operandi? Regarding this point, Wile says that "the occurrence of epithelioma following the use of arsenic is in all probability the result of several factors; in the order of their importance they are:

"(a) The chemical action of arsenic acting as a protoplasmic irritant, leading to the production of tissue especially liable to malignant degeneration.

"(b) The irritation and trauma to which precancerous lesions (keratoses) are constantly subjected.

"(c) The occurrence in most of the subjects of arsenical cancer of a pre-existing chronic disorder and abnormality of the epithelial covering.

"(d) In addition to these factors, the suggestion that in arsenical cancer the changes may be due to chemical alteration of the cell rendering it more sensitive to solar activity seems worthy of further thought and investigation."

Resume

(1) Arsenic internally, particularly pentavalent arsenic, may cause chronic skin eruptions upon which epitheliomas may develop.

(2) Keratoses usually precede the cancerous growths.

(3) The squamous-cell cancer is usually found in these cases.

(4) It is not known whether the direct chemical action of the arsenic on the cell is the exciting factor in the cause of the cancer, or irritation of tissues already altered by arsenic.

(5) Physicians should warn their patients against the repeated internal use of arsenic. This remedy should not be prescribed too freely.

(6) Arsenical keratoses may appear within six months

of the taking of arsenic or they may not occur until many years have elapsed.

(7) Most keratoses following arsenic appear on the hands and feet, although occasionally they occur on the trunk and other parts.

(8) Carcinoma most frequently follows arsenical keratoses on the hands or feet.

(9) As shown by Fouss, in more than one-half of the reported cases the carcinomatous foci were multiple.

Sebaceous Cyst

Ricker and Schwalbe reviewed the literature up to 1914 and found 43 cases of sebaceous cysts in which carcinoma developed in the cyst walls. In 17 of these there was ulceration. The malignancy was seen mostly in cysts on the face and scalp. While the age incidence varied between 20 and 70, most of the malignant growths occurred in persons over 60 years of age.

Caylor in a recent report of 236 cases of sebaceous cysts seen at the Mayo Clinic found 12 instances where there was a malignant growth. Most of his cases of malignant change were in lesions on the head and neck. The ages of these patients varied from 38 to 82 years. Four of the cases presented ulceration. Caylor found on microscopic study that 10 of the epitheliomas were of the squamous-cell type and two of the basal-cell variety.

I have seen this complication twice during the past years. One patient was a woman, aged 81 years, who had a sebaceous cyst in the left temporal region for twelve years. This had grown slowly in size until about one year ago when an ulceration appeared on the surface. On examination the patient presented a globular swelling extending from the outer edge of the left eyebrow to the hairline of the temporal region. This globular mass was ulcerated on the surface, was dry and had a ragged edge. The entire mass was excised by means of the high-fre-

quency cutting current. A microscopic study revealed a large sebaceous cyst, and growing in its wall was a prickle-cell carcinoma which had presented itself as an ulceration on the surface.

Chronic Ulcers and Fistulae

While chronic ulcers of the legs associated with varicose veins and often called varicose ulcers are frequently seen in persons at the age when carcinoma is most frequent (40 to 60 years), yet cancer supervention in these ulcers is extremely rare.

When one considers that many thousands of cases of varicose ulcers have been observed in clinics and private practice in the last fifty years, and that a search of the literature reveals some sixty odd cases of cancer supervening on such ulcers, it can be concluded that this complication is most infrequent.

Volkmann, Gottheil and Knox in comprehensive articles on this subject emphasize this surprising fact. They point out that in varicose ulcers all the conditions are seemingly favorable for the development of cancer such as a low-grade inflammatory process, chronicity, irritation from various stimulating applications used in treatment, the age of the patient, associated circulatory disturbances, foul and necrotic secretions and the frequency of years of neglect. The average duration of the ulcer preceding the development of the cancer was twenty years. The squamous-cell variety of cancer was found in every reported case.

A consideration of the above facts leads one to the following questions:

(1) If the above conditions were found on the mucous membranes, such as the mouth and tongue, one would expect a cancerous growth in a comparatively short time. What is the reason, therefore, for the extreme rarity of malignancy in the many thousands of varicose ulcers?

(2) Does the impaired circulation act as an inhibiting influence on the development of cancer?

(3) Is there a comparative local tissue immunity?

There have been reported about 50 cases of carcinoma following fistulae, most of which have been about the ankles and calves. One of our own cases occurred in the anal region, following a long-standing anal fistula. The growth was rapid, and metastases occurred with subsequent death. Fistulae occurring on the lower extremities are usually associated with a long-standing osteomyelitis, sinus formation and subsequent ulceration followed by carcinoma.

There have been a few isolated reports of cancerous growth in decubitus ulcers and also in pellagrous ulcers of the skin. These, however, have been extremely rare. Bloodgood reported his case of cancer in a lesion of blastomycosis. This also is a rarity. Wise mentions the occurrence of cancer in the ulcerations that may be present in long-standing atrophic patches of acrodermatitis chronica atrophicans on the legs.

Lupus Erythematosus

Carcinoma occasionally occurs in lupus erythematosus, but much less frequently than in lupus vulgaris. From a fairly complete review of the literature the following conclusions may be drawn:

(1) Carcinoma may develop in untreated active lupus erythematosus lesions.

(2) The combination or association of cancer with lupus erythematosus may be purely a coincidence.

(3) Carcinoma may develop in old scars of previously untreated lupus erythematosus.

(4) Carcinoma may develop in lupus erythematosus which previously had been treated by irritants such as roentgen rays, radium, chemical applications, etc.

(5) With the exception of one or two isolated cases, reported as basal-cell epitheliomas (and these are ques-

tionable), the carcinoma complicating the lupus erythematosus was always of the prickle-cell type.

(6) In nearly all of the cases reviewed this complication occurred in areas about the face and scalp.

(7) Its occurrence is usually in long-standing lesions.

(8) While a review of the literature reveals approximately 60 cases of carcinoma complicating this disease, one gleans from reading discussions that many cases have been observed but not reported.

(9) While Wander has reported four carcinomas in his group of 110 lupus erythematosus patients, others have not seen it as frequently.

(10) Since the carcinoma which develops on a lupus erythematosus is usually of the prickle-cell type, this complication is serious.

Cicatrices

It is well known that carcinomas have arisen in old scars of lupus vulgaris, syphilis and lupus erythematosus. If we exclude these diseases the occurrence of cancer in old scars is not frequent. Scars resulting from any form of trauma may be a menace, but small superficial scars and keloids practically never give rise to cancer. Large scars resulting from third-degree burns are those most likely to develop carcinomas. These cancers are usually of the squamous-cell variety. Treves and Pack recently published a thorough and painstaking study of the development of cancer in burn scars. They gave an analysis and report of 34 cases of skin cancer which resulted from various types of thermal injuries.

Cutaneous Horns

Cutaneous horns are peculiar horny growths, which are characterized by excessive and progressive keratosis. They are most frequently found on the scalp and face, and less often on the buttocks, penis, scrotum and nails. Lebert

collected 109 cases of general distribution and Wilson 90 cases. Cutaneous horns are usually single, but may be multiple. They vary in size from small pointed nodules to large excrescences. Rodriquez reported a horn in the scalp 14 inches in circumference. In the beginning the growth is usually rapid but later becomes slow and intermittent, and after reaching a certain size usually remains quiescent. The horn may then become permanent or detached followed by the regrowth of a new horn. Owing to the irritation caused by the presence and movement of the horn, the base of which is entirely cutaneous and movable, the warty base readily assumes malignant changes. Lebert found this occurrence in 12 per cent of his cases. Cutaneous horns and epitheliomas have the same favourite sites, i. e., areas of predilection for seborrhea. Sutton is of the opinion that there is a distinct relationship between the "warty" form of seborrheic keratosis and certain types of cutaneous horns. A review of the literature readily convinces one that epithelioma is a frequent complication of cutaneous horns.

Bowen's Disease

Since Bowen described an unusual form of dyskeratosis as a "precancerous dermatosis," much controversy has arisen as to the correctness of his assumption that the condition was precancerous rather than cancerous. Lately this subject was reviewed by Fraser and Wise, who consider this condition an intra-epidermal carcinoma. I shall use their material freely in drawing the following conclusions:

(1) Microscopic evidence proves Bowen's disease to be a distinct entity with histological features peculiar to itself and indicative of intra-epidermic carcinoma.

(2) Many cases reported as Bowen's precancerous dermatosis are examples of a peculiar form of epithelioma usually of the basal-cell variety, but at times prickle-cell and more rarely of the mixed basal and prickle-cell type.

(3) This error was made because dyskeratosis occasionally occurred in certain lesions of so-called multiple superficial flat epitheliomas of the skin.

(4) A definite diagnosis of Bowen's disease cannot be made on clinical evidence alone but requires microscopic study.

(5) Up to 1925 only 12 of the 34 cases reported as Bowen's disease had stood the test of clinical and histological scrutiny.

(6) There is evidence (a) that the lesion in Bowen's disease may remain indefinitely within the confines of the epidermis, or (b) it may break through the basement membrane and become transformed into an infiltrating carcinoma.

(7) The primary and essential change in the Bowen lesion is not a dyskeratosis, but a disturbance of epithelial growth in which the cells have undergone the changes of malignant neoplasia.

(8) As Bowen's disease is cancer, the term "precancerous" as applied to the lesion by Bowen and Darier is illogical and should not be used.

(9) Other types of carcinoma may arise independently and may be associated in the same person having the Bowen lesion.

(10) Bowen's lesion occasionally becomes an infiltrating carcinoma of the squamous-cell type.

(11) If one restricts the meaning of the term "carcinoma" to an infiltrating neoplasm, Bowen's lesion is not a carcinoma. If, on the other hand, the definition of the term can be extended to include a lesion in which the cells have undergone all the changes constituting malignancy, but remain in situ, there is justification for designating the Bowen lesion as an intra-epidermal carcinoma.

(12) The so-called Bowen disease must be treated with the same thoroughness as the resistant type of flat epithelioma of the skin.

Papilloma of the Tongue

Papilloma is one of the commonest of the simple tumors of the tongue and may appear at all ages. Although occurring in other areas it is usually located on the dorsum or papilla-bearing area. Occasionally papillomas are found on the floor of the mouth, inner surfaces of the cheeks, lips, and on the palate. They may be single or multiple. Microscopically they resemble a common wart. They may be congenital, but most frequently seem to be caused by various forms of irritation, such as tobacco and bad teeth. Many observers are in general agreement with Ewing who states: "While some papillomas long remain benign and enjoy a limited growth, there is a strong tendency towards malignant change, which is indicated by increasing growth, induration and fixation of the base and ulceration." When cancer occurs it is of the squamous-cell variety.

Xeroderma Pigmentosum

This rare malady most often begins in early childhood, and is considered to be due to an inherited peculiar susceptibility of the skin to the sun's rays and other forms of light. The exposed areas of the body are those first affected. This disease is characterized by a syndrome of symptoms not unlike that of chronic radiodermatitis, i. e., hyperpigmentation, telangiectasis, sclerotic and atrophic whitish areas, keratoses and malignant growths. While this disease is incurable, patients may live to be thirty or more years of age. Basal-cell cancer is the type usually reported, but other neoplastic growths have also been found. The treatment is palliative. All keratoses and ulcerations should be destroyed as early as possible, preferably by some form of high-frequency current such as electrocoagulation.

Inflammatory Dermatoses

Most observers are in accord with Hazen, who says: "Eczema, lichen planus, and psoriasis occasionally give

rise to cancer of the skin, but in the vast majority of the cases reported it is probable that either arsenic or roentgen ray was the true cause."

Paget's Disease of the Nipple
(*A Manifestation of Intraduct Cancer*)

I shall report here three cases of Paget's disease of the nipple in which each affected breast presented a true intraduct carcinoma, as shown on microscopic study of serial sections. There were no palpable tumors in these mammary glands. It is significant that the lesion on the nipple of one of these carcinomatous breasts was of only one month's duration.

The observations in these cases substantiate the reports of Cheatle, Pautrier, Fraser and others who gave cogent reasons for removing Paget's disease of the nipple from the realm of the "so-called precancerous dermatoses" and putting it in the class of a true cancer.

Paget's disease of the nipple is most frequently seen in women over 40 and is usually unilateral. Most often it begins as a mild eczematoid condition of the nipple which may spread over the areola and even part of the breast. Later it may become ulcerated or erosive. In the more advanced stage there may be retraction of the nipple. Occasionally before any dermic lesion is seen a serous exudation may be present on the nipple as a forerunner of what is to follow.

Three Case Reports

Case 1—Mrs. R. C., a patient of Dr. Edward P. Swift, aged 45 and the mother of two children, was first examined by me Jan. 14, 1929, when she complained of a slight irritation of the right nipple of one month's duration and said that the nipple had looked perfectly normal before the symptoms began.

On examination of the right breast, an eczematous con-

dition involving the entire right nipple was found. The surface of the involved nipple was eroded and appeared flatter than the normal one. The affected nipple was slightly more firm but was freely movable. The areola appeared to be normal. No tumor masses were present in the breast or axilla on palpation. A section from one corner of the nipple, taken for microscopic study, revealed the typical changes of Paget's disease. This microscopic diagnosis was concurred in by Drs. Ewing, Fraser and Satenstein.

Two weeks later the entire breast was removed. A microscopic study of numerous serial sections of part of the tissue and ducts revealed a glandular carcinoma in one of the ducts about 2 mm. from the surface.

Through and through vertical serial sections of the breast were also made according to Cheatle's method. These sections did not reveal any deeper intraduct carcinoma.

CASE 2—Mrs. R. D., aged 61, first came to the Skin Clinic of the New York Post-Graduate Medical School and Hospital, May 22, 1929, at which time she complained of an abnormal involvement of the right nipple of two years' duration.

On examination the right nipple and surrounding areola were found covered with a well defined, somewhat irregular, slightly thickened erythematous plaque. The right nipple was smaller than the left and was slightly infiltrated. There were no masses palpable in the breast and no axillary gland enlargement.

A microscopic study of sections by Drs. Satenstein and Fraser showed typical Paget's disease with an intraduct carcinoma.

CASE 3—Mrs. S., aged 60, a patient of Dr. Oleynick, presented an eczematous and retracted condition of the left nipple and areola of two years' duration. There were no palpable tumors or enlarged glands. A microscopic

study of a biopsy of the nipple and deeper tissue by Dr. James Ewing revealed a typical Paget's disease with an intraduct cancer.

Dr. James Ewing, who carried out the microscopic studies of the breast in cases 1 and 3 made the following statement in a personal communication:

"It is now pretty well agreed that Paget's disease of the nipple is so uniformly associated with carcinoma of the ducts of the breast that treatment must be designed to deal with a duct cancer. These small duct cancers may be found in any part of the breast and they are sometimes multiple. A palpable tumor may not be felt."

I agree with those who believe that Paget's disease of the nipple is a true cancer from the beginning; that, as indicated above, the Paget cells found in the epidermis are true cancer cells. I am also inclined to believe with Masson and Pautrier that Paget's disease of the nipple is an epithelioma that has arisen in the first milk ducts near their mouths. Finally, I too am strongly of the opinion that Paget's disease should never be considered a precancerous lesion but always a carcinoma of the nipple, symptomatic of a deeper carcinoma of the breast, and that early and total removal of the mammary gland is always indicated.

Extra-Mammary Paget's Disease

While Paget's disease has been described in regions other than the nipple by numerous observers (Pautrier mentioned 28), none of them have proved by histological examination that this disease was present without a carcinoma involving the deeper structures such as sweat glands, pilosebaceous apparatus or other subjacent glands.

Of 22 reports of extra-mammary Paget's disease, Pautrier found that 13 were either true basal-cell epitheliomas or were associated with subjacent glandular carcinoma. Several were diagnosed on clinical grounds only. Therefore these latter reports are valueless. The remaining

few cases showed no "Paget cells" microscopically, and the histological reports otherwise did not conform with those of Paget's disease. If this condition does exist it is doubtful whether it is present without a carcinoma of the subjacent tissues.

Basal-Cell Epithelioma

A large number of chronic lesions of the skin in individuals past 40 years of age are found to be basal-cell epitheliomas. They frequently develop on seborrheic keratoses. Basal-cell epitheliomas may differ greatly in their clinical appearance. They may occur at any site over the body. They may be superficial or deep, nodular or ulcerating. It is interesting to note, however, that about 80 per cent of these lesions occur about the head and neck. The method of treatment to be chosen depends upon the character of the lesion and its location. The large majority of basal-cell epitheliomas can be cured especially when treated early. However, lesions which have been present for a long time and which have invaded bone and cartilage may prove much more resistant to radiation and require more intensive treatment.

MacKee reported a large number of basal-cell epitheliomas treated entirely by roentgen rays. His results were equal to those obtained by other methods of treatment. In over 400 cases he had 87 per cent permanent cures in unselected cases and 91 per cent permanent cures in selected cases. Hazen reported his results of 200 cases treated entirely with roentgen rays, with permanent cures of 86 per cent in unselected cases and 93 per cent in selected cases after observation of one to eight years. Most of the failures reported in both MacKee's and Hazen's series were in lesions of long duration with involvement of bone or cartilage.

Equally good results have been obtained by radium especially in the last five years. Quick reported 800 cases of basal cell epitheliomas of the face, 95 per cent of which have had complete regression. Quigley treated 140 cases

of the face with 15 failures. Morrow and Taussig treated 322 cases with 113 cures under one year, 186 over one year, 13 still under treatment and 10 failures.

My results with irradiation have been similar to the above and the results with roentgen rays or radium were practically of equal value. However, radium was successful in a few cases where roentgen rays had failed. At times radium can be more easily utilized than roentgen rays, especially in such areas as the inner canthus of eye and the alæ of the nose. On the other hand roentgen rays are more widely available and distinctly less expensive.

I have used the unfiltered roentgen rays frequently for basal-cell epitheliomas. The following were standard factors: three milliamperes, one hundred kilovolts (6 in. sp. g.), eight inch distance from target to skin, time five or six minutes, i. e., 2½ or 3 skin units. This exposure may be repeated two weeks after all reaction has subsided (6-8 weeks); or a dose of lesser intensity given according to the progress or size of the lesion. Usually two such treatments were sufficient for a cure. The larger lesions were routinely destroyed by electrocoagulation before roentgen ray therapy. My experience has been that preliminary destruction by electrothermic methods increased the number of cures and decreased the amount of radiation necessary. One-eighth to one-quarter of an inch of normal skin about the lesion was included. This is an important factor in preventing recurrences.

Lesions involving the cartilage of the ear or nose are completely destroyed by electrocoagulation or excised with the high-frequency knife; followed by two skin units of unfiltered roentgen rays or the equivalent dosage of radium element or radon applied to the site of the lesion. In this manner severe radium or roentgen-ray reaction is avoided in the cartilage, and healing is much more rapid. Skin lesions involving the bone require removal of the diseased bony tissue.

Lesions of the eyelids not involving the conjunctiva in selected cases may be treated successfully with roentgen

rays or radium. If the eyeball is in the line of the rays the eye must be protected with a brass eye shield inserted beneath the lids. Supersoft roentgen rays (Grenz Rays 2 AU) have been used with success in epitheliomas of the upper eyelid but they have failed in lesions of the lower eyelids.

Radium element or radon used in the form of plaques or packs for surface applications accomplish the same results as roentgen rays in the treatment of basal-cell epitheliomas. The average lesion of this type may be cured with radium or radon. The following treatment is given: a full strength plaque filtered with two millimeters of aluminum and one layer of rubber dam giving a dosage of 40 to 60 milligram hours per sq. cm. for the small lesions and 40 to 50 milligram hours per sq. cm. for the larger lesions (larger than two square cm.). For the more deeply infiltrated lesions a filter of 2 mm. of brass is used giving a dosage of 60 to 80 mgm. hours per sq. cm. Two to four millimeters of normal skin about the lesions are included. The surrounding skin should be protected with lead plates having windows the size of the area to be treated. The plaque with the filters is then applied directly to the lesion and secured in place by adhesive. Double faced adhesive is of value in maintaining good approximation. Often one such treatment is sufficient for a complete regression of a basal-cell epithelioma. When the regression is not complete the treatment may be repeated two weeks after all reaction has subsided. Other methods of applying radium may accomplish equally good results in experienced hands.

Prickle-Cell Epitheliomas

Prickle-cell epitheliomas present a more difficult problem than the basal-cell type. They grow more rapidly, may metastasize early, and usually are more resistant to radiotherapy. A complete destruction of every cancer cell is important and must be accomplished early and rapidly. This type of cancer may occur at any site. They

often develop on such lesions as senile, arsenical, and tar keratoses, smokers' patches, and other types of leukoplakia. They are frequently seen on the lip, tongue, buccal mucosa and floor of mouth. I have observed that the majority of epitheliomas of the extremities are of the prickle-cell type, especially those on the dorsum of the hands. Recently I reported a number of prickle-cell epitheliomas which had developed in senile keratoses.

The treatment of prickle-cell epitheliomas varies depending on the location and the character of the lesion. A microscopic study is necessary in each case, for proper therapy cannot be given without knowing the type of lesion, degree of malignancy and its probable radiosensitivity. The information often to be gained by histologic study warrants the danger of making a biopsy of a neoplasm. Ewing warns against indiscriminate biopsies but says, "the removal of a small carefully selected portion of a readily accessible tumor seldom results in any harm." I believe that the dangers of a biopsy are overestimated.

This discussion of treatment is limited to localized lesions without apparent glandular involvement. The dermatologist is usually not equipped to treat those cases that present involvement of the glands. The latter are better handled by a surgeon experienced in malignancy and in collaboration with a radiotherapist.

Early prickle-cell epitheliomas of the trunk or extremities can be treated successfully by radiation alone. Most often, however, it is desirable first to remove the lesion surgically or to destroy it by electrocoagulation. Following this radium or radon should be applied. When radium is used intensive gamma ray radiation should be employed. Even though there be no apparent involvement of the adjacent glands a series of prophylactic exposures of roentgen rays filtered through three millimeters of aluminum should be given, i. e., erythema doses at intervals of two months for three treatments.

In the treatment of prickle-cell epitheliomas with radium, the required doses were given over a period of 4

to 8 days, giving equal time each day during this period after the method of Regaud. Continuous treatment with large doses over a period of several days gave satisfactory results.

When it was found preferable to implant radon seeds into the tumor, gold seeds were used as they could be left in the tissues permanently, each millicurie thereby giving 133 millicurie hours of treatment.

The lesions over cartilagenous areas, particularly the ears, are very resistant to irradiation. These lesions should first be thoroughly destroyed by electrocoagulation and then followed by irradiation. Much better results have been obtained in these cases since adopting this method of destruction, especially when the cartilage was involved.

Lesions in the inner canthus of the eye which are usually of the infiltrating type respond well to radium treatment when the growth is first destroyed by electrocoagulation.

Lip lesions are much more serious than those of the glabrous skin. They grow more rapidly and may metastasize early. They may be papillary, ulcerating or infiltrating. The infiltrating type is the most dangerous for it metastasizes more quickly. The papillary type responds more rapidly to radiotherapy. Early superficial localized lesions of the lip can readily be cured with surface applications of either radium plaques or tubes. However, I believe it best to destroy these lesions first with electrothermic methods and then to apply full strength radium plaques to the involved area; and to give 80 to 100 mgm. hours per sq. cm. through a filter of 2 mm. aluminum. When these tubes are used with a filter of 0.5 mm. of silver 80 to 100 mc. or mgm. hrs. are given to each sq. cm. The area to be treated should always include about 5 mm. of tissue beyond the lesion. The tissue outside the area to be treated should be protected by proper screening. Prophylactic exposures of roentgen rays should always be

given to the lymphatics which drain the lip area even though there be no evidence of involvement.

Lip lesions which are more deeply infiltrated require more intensive therapy. In addition to the above surface applications, gold radon seeds may be permanently buried in the lesion using one seed for every cubic centimeter of tissue treated. These seeds may be 1 to 1.5 millicuries each, depending upon the reaction desired. I have never seen any deleterious effects as a result of the permanent implants acting as foreign bodies. This combined surface and interstitial method of applying radium will usually produce complete regression of the lesion.

The highest percentage of good results have been obtained by first excising the lip epithelioma widely with the high-frequency knife, following which the site of the lesion was treated by an erythema dose of gamma rays of radium by surface applications or by the implantation of gold seeds as described above. In a few early cases excision alone with the high-frequency knife was sufficient to cure. The patient should have the additional safety factor to be derived from radiotherapy in all of these cases. When surface applications only are employed, the dose can be considerably increased by cross-firing through three portals of entry, i. e., applying an applicator over lesion, on the mucosa, and on the skin externally. As was mentioned before prophylactic doses of roentgen rays were always given to the lymphatics draining the involved area.

Regaud utilizes wax molds for surface applications. Platinum tubes of 0.5 mm. wall thickness and containing 5 to 10 mgm. of radium are approximated to the external surface of the mold at one centimeter distance. The radiation is given over a period of 5 to 8 days. His results in lip cases have been good. He reported cures of 98 per cent of operable cases without glands, and 92 per cent of operable cases with glands. In cases of doubtful operability including those with glands he had 72 per cent cures.

Quick uses heavily filtered radium or radon at a distance

of one cm., or gold filtered radon seeds interstitially. His results equal those of Regaud.

Lesions of the tongue, floor of the mouth and buccal mucosa differ widely in regard to malignancy and radiosensitivity. Metastases occur increasingly according to the location as follows: anterior tongue; posterior tongue; infralingual; and floor of the mouth. Metastases are greater from the tongue and floor of the mouth than from the lip and the glands involved are deeper. For the mouth lesions, the interstitial method of irradiation with or without electrothermic methods as indicated has given the most satisfactory results. Tongue lesions may be treated by interstitial irradiation with gold radon seeds implanted permanently into the tumor area and across the base of the tongue (to block the draining lymphatics). Prophylactic roentgen therapy should be given to the draining lymphatics of the cervical region. I usually use 1 or 2 mc. gold seeds and place one seed to each cubic cm. in and around the tumor area and four to six such seeds in the base of the tongue. The reaction may be severe but necrosis as a rule does not occur. Quick uses gold seeds interstitially and the radium pack (4 gm.) for external irradiation giving as much as 10,000 to 12,000 mc. hrs. to each side of the neck at 6 cm. or 10 cm. distance and in addition high voltage roentgen rays. He believes that the tissue will tolerate a larger dose of external irradiation when both radium and roentgen rays are used and that radium has the greatest effect on cellular areas and roentgen rays the greatest effect on fibrous areas. By this combined method of interstitial and external irradiation he gives from 2 to 10 skin erythema doses to the tumor area in 4 to 8 days according to the degree of malignancy and radioresistance of the tumor.

For tongue lesions Regaud uses platinum needles of varying length with a wall of 0.4 mm. thickness. These needles contain radium or radon and are inserted into the tumor area and surrounding tissue. For the base of the tongue and lymphatics external irradiation is given by

means of molds and packs of radium at a distance. This treatment extends over a period of 5 to 8 days.

Epithelioma of the penis which is usually of the prickle-cell type responds well to roentgen rays and radium in early cases. One to three per cent of all cancer in the male is found on the penis. Two types are seen: the papillary and the flat infiltrating. They usually begin as a small indurated area and soon present a small central ulceration. If treatment is begun before the deep tissue is invaded an early cure is to be expected. When the growth has spread past Buck's fascia the lesions do not respond as well to radiation and a certain number require amputation of the organ. This is best accomplished by electrothermic methods. For small lesions of recent development I have used full strength plaques of radium with a filter of 2 mm. aluminum giving 80 to 100 mgm. hrs. per sq. cm. Prophylactic roentgen rays are given to the inguinal glands. Pfahler and Widmann reported 10 cases of cancer of the penis treated by radiotherapy and electrocoagulation, with 9 cured from five to twelve years. They believe that irradiation of the glands gives superior results to resection. Dean reported 75 cases of epithelioma of the penis. None of his cases occurred in individuals who were circumcised in infancy. He believes the tight prepuce to be the most important factor. He uses radium for the primary lesions and roentgen rays for the glands in the groin. The primary lesions receive 1,200 mc. hrs. per sq. cm., at one cm. distance with the radium in silver tubes of 0.5 mm. walls. Dean uses a radium pack (4 gm.) for groin metastases giving 9,000 mc. hrs. at 6 cm. distance with 0.5 mm. silver and 1 mm. brass. This is followed in three to four weeks by block dissection. He reported good results with radium alone in lesions less than two centimeters in size and those larger he found required combined surgical measures and irradiation. In most of his cases radical amputation was not necessary.

Epithelioma of the vulva is not common and usually occurs in those past fifty years of age. When treated

early, the prognosis is favorable. When operable, these lesions should be removed by wide excision, with the high-frequency knife and radon seeds implanted throughout the area. Deep roentgen rays are given to the groins. Rentschler reported 71 cases which were treated by excision of the primary mass and resection of the glands of the groin. Radium and roentgen rays were given to the site of the primary lesion and to the groins. Forty-four died, 17 are living and 13 are free of the disease. As a measure of prophylaxis all cases of kraurosis vulvae should be treated by radical excision. This gives prompt relief from all symptoms and prevents the development of epitheliomas. Roentgen rays and radium fail to influence the course or symptoms of kraurosis vulvae and are contra-indicated.

Basal-Squamous Cell Epithelioma

"Basal-squamous cell epithelioma" is a term used to describe the transitional form that occurs between the basal-cell and the squamous-cell epithelioma. I have been able to study one case that fits into this group. The following conclusions drawn by Montgomery from his studies of fifteen cases which he defined as basal-squamous cell epithelioma are as follows:

"In a series of basal-cell epitheliomas diagnosed clinically as such, from 15 to 20 per cent on microscopic examination will probably prove to be transitional in character."

"Basal-squamous cell epithelioma, in the majority of cases, is relatively resistant to roentgen-ray and radium treatments as compared with basal-cell epithelioma. Radiotherapy should be used only as a last resort in the treatment in these cases."

"Surgical treatment, with an unusually wide excision because of the insidious infiltration of the tumor cells, is indicated whenever possible."

There is no doubt that all of us have encountered what appeared to be typical basal-cell epitheliomas which were

most resistant to intensive doses of roentgen rays and radium. Perhaps some of these resistant lesions belonged to the type described by Montgomery who stated that this transitional form occurs frequently and on account of its tendency to metastasize, the prognosis is serious as compared with basal-cell epithelioma.

Transitional-Cell Epidermoid Carcinoma

The predominant clinical features of transitional-cell epidermoid carcinoma are: usually a small primary lesion of the base of the tongue or tonsil; early metastases with wide dissemination; and rapid response to irradiation.

Ewing, Quick, and Cutler who studied a large number of intra-oral epidermoid carcinomas found that a certain percentage responded more rapidly and more completely to irradiation than the others. These tumors were found to possess other characteristics, i. e., usually a small primary lesion, early metastases and pathological characteristics which differed from other epidermoid carcinomas. Quick and Cutler termed these growths "transitional-cell epidermoid carcinoma."

The most common sites of these lesions are the tonsil, base of tongue and nares. The appearance of the primary lesion is more or less characteristic and differs from that of a primary squamous-cell lesion. The transitional-cell lesion is flat and presents a finely granular, velvety surface which looks like an erosion of the mucous membrane rather than an ulceration. Squamous carcinoma usually presents an elevated indurated lesion with a depressed ulcerated center and has a coarsely granular appearance. The primary transitional-cell lesion is frequently small or indistinguishable and often the first sign of disease is a swelling in the neck. Many cases have been erroneously diagnosed as bronchiogenic carcinoma, endothelioma, or lymphosarcoma. The transitional-cell neoplasm must always be considered before making a diagnosis of primary disease of the cervical lymph nodes.

Transitional-cell carcinoma is a highly cellular malig-

nant tumor. The cells are small, uniform in size, with large hyperchromatic nuclei and scanty cytoplasm growing diffusely. Adult squamous characteristics such as cornification, spines, and pearl formation are absent.

The marked radiosensitivity which leads to the discovery of these tumors is the important factor in their treatment. They should be treated by radiotherapy because of their high radiosensitivity and high grade of malignancy and must be treated early. The primary lesion may be treated by gold radon implants distributed uniformly throughout the tumor. This treatment has been very satisfactory and most of the tumors have regressed rapidly and without necrosis. The treatment of the metastatic lymph nodes with high voltage roentgen rays and radium has resulted in a complete regression in most cases. Quick reported cures of some cases treated entirely with external irradiation by combining high voltage roentgen rays and the radium pack (4 gm.). By this method one of his cases received between two and one-half and three erythema doses to the glands and primary lesion by external irradiation and has been without evidence of disease for over three years.

Primary Sarcoma of the Skin

Sarcomas are the least common of the cutaneous malignant neoplasms and for this reason very little definite information is obtainable. They vary considerably as to the clinical type, histologic structure, degree of malignancy, and likewise in their response to radiotherapy. They may be either single or multiple. The large majority of primary sarcomas of the skin are of the spindle-cell or fibrous type. The fibrosarcoma is the most benign. They respond poorly to radiotherapy and complete surgical excision offers the best prognosis.

The spindle-cell type may be composed of large or small cells and varies as to the amount of cellular elements. The spindle-cell sarcoma may be radiosensitive when highly cellular and radioresistant when composed almost

entirely of stroma. Therefore, the cellular type should be treated with roentgen rays or radium and the fibrous types by surgical excision with irradiation before and after removal. Recurrences frequently occur and pulmonary metastases are the end results in many cases.

The giant-cell sarcomas (usually develop from the tendon sheaths) are least malignant and very radiosensitive, roentgen rays and radium being almost specific in these lesions.

Under the name of neurogenic sarcoma Ewing has classified a group of tumors commonly designated as fibrosarcomas, spindle-cell sarcoma and fascial sarcoma. These lesions usually arise about the arms, legs, popliteal spaces, abdominal and chest wall as small movable subcutaneous nodules. Quick and Cutler reported 75 cases of neurogenic sarcoma most of which had from one to three recurrences after local removal. Operable cases were given irradiation and widely excised with only a few cures. In 10 cases, amputation of the extremity resulted in 5 cures and 5 deaths from pulmonary metastases. Only 17 had a complete regression in their series of 75 cases.

Dermatofibrosarcoma was described by Darier in 1924 and several cases have been reported since. These tumors are usually of the acellular spindle-cell variety, are relatively slow growing and do not metastasize. They are radioresistant and have a marked tendency to recur when excised. The most successful results have been obtained when they have been very widely excised. Senear reported two cases treated by surgical excision without recurrence.

Melanosarcomas are exceedingly rare lesions and arise from pigmented lesions in the cutis (Bloch blue nævus). Their treatment is identical with that given for melanocarcinoma.

Lymphosarcomas usually arise in a single chain of lymph glands but may arise from lymphatic tissues elsewhere. They are exceedingly malignant. Their response

to radiotherapy is very rapid. Recurrences are frequent. Often metastases although not apparent have occurred before therapy was instituted. One of my cases of lymphosarcoma treated two and one-half years ago has had no recurrence. This patient was a man 60 years of age who had a lemon-sized stony hard mass of twelve years' duration on his chin. There was a nut-sized firm gland on the left side of his neck near the chin. The above microscopic diagnosis was concurred in by Doctors Ewing, Satenstein and Fraser. The lesion and gland were removed by the high-frequency knife, following which the base was electrocoagulated. The next day high voltage roentgen rays in erythema doses were given to the neck lymphatics and site of the lesion. This was repeated twice at intervals of two months.

The preferable therapy for lymphosarcomas is by irradiation alone, but due to the unusual hardness of this mass, combined surgery and radiotherapy was indicated in this case.

The best results in early sarcomas are obtained by a combination of radiotherapy and surgery. The dose required with either roentgen rays or radium is the same as that given for prickle-cell epitheliomas. Following the initial radiotherapy, if there is considerable regression indicating radiosensitivity, they may be treated entirely by this method but the more radioresistant lesions will require surgical excision and postoperative radiotherapy.

Summary

1. It has been shown that over twenty different skin conditions may be precursors of cancer.

2. The incidence of cancer supervention in such dermatoses has been discussed.

3. The early recognition by the general practitioner and the judicious treatment of those dermatoses which may lead to cancer would aid in lowering the mortality rate in this disease.

4. The treatment of the various types of cutaneous malignant neoplasms has been outlined.

5. Those conditions which had a high degree of sensitivity to irradiation and which could be satisfactorily treated with irradiation alone were noted.

6. The lesions which should be treated by some surgical method combined with irradiation have been discussed.

7. The information often to be gained by histologic study warrants the danger of making a biopsy of a neoplasm. In this way the degree of malignancy and its probable radiosensitivity may be determined. The removal of a small carefully selected portion of an accessible tumor seldom results in any harm.

MORE COMMON DISEASES OF THE TEETH AND JAWS

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The general medical practitioners as well as the medical specialists are probably less familiar with conditions of the jaws and teeth than with those of any other part of the body, for which reason a discussion of the more common diseases involving these structures is rather timely. Because a detailed study would involve a good deal of time, an attempt will be made to mention only the most important conditions and discuss them briefly.

In former years, a goodly percentage of the medical and dental profession believed that almost any ailment could be cured or at least improved by the removal of infected teeth. At the present time the problem of oral focal infection is more conservatively treated and, therefore, a more sane mode of procedure indicated where an oral focus is suspected. First of all there must always be co-operation between the medical practitioner and the dentist or oral surgeon. The teeth and jaws will have to be completely x-rayed, pulptested and transilluminated and all teeth and roots not amenable to dental treatment removed if there is no objection on account of the patient's general condition. So much should be done for every patient. If, however, not only an oral focus is suspected, but if the patient is also suffering from a disease which is known to be caused by a focus or improved by the removal of the same, then as a last resort, all devitalized teeth otherwise in good condition from the dental standpoint as well as teeth showing gingival disturbances which cannot be cured, will have to be sacrificed. Even in those cases where a doubt exists as to the connection be-

tween an oral focus and the patient's ailment, one cannot take the chance to leave such teeth in position, and this radical procedure will have to be adhered to.

Pathological changes at the apical end of a tooth in the form of a thickened apical peridental membrane (so-called granuloma) and cysts in the same region do not always indicate that such teeth must be removed. In a large number of cases such teeth remain useful for many years after the dentist has properly treated and filled the root canals and the apices as well as the granuloma or cyst have been surgically removed (Root Amputation). Such procedure is generally indicated in cases where no suspicion of focal infection is present, although cures of focal disease have been reported with this conservative method. Curettage of the apical area after extraction is always indicated because it is well known that such granulomas may develop into cysts if epithelial rests are present in the peridental membrane and because the extraction of such a tooth alone would not prevent cyst formation.

Cysts developing from devitalized teeth as well as the follicular cyst forming around the crown portion of malposed teeth are quite frequently seen in the jaws and will, if they are permitted to grow, destroy not only the surrounding bone, but also the usefulness of adjoining teeth. In the maxilla they will at times displace the antrum, although they never communicate with the antrum unless an acute infection within the cyst finds its way through a thin—at times only membranous wall—into the maxillary sinus. As a rule, diseases of the maxillary sinus belong to the field of the rhinologist. Only in those cases where the antrum is involved through some disease of the teeth or the surrounding bone it becomes the duty of the oral surgeon to treat the antrum.

Malposed teeth present a problem about which the medical practitioner should be better informed. Although such teeth do not become infected while they are unerupted, the possibility of their causing nervous disturb-

ances must be kept in mind. For that reason such teeth should be either placed into normal position—for which purpose the orthodontist and oral surgeon will have to co-operate with the general dental practitioner—or they should be removed. The operation for their removal should be advised in the young because at this time the roots of these malposed teeth are not fully formed and the bone will not be found as hard and dense as in adult life. Infections from partly erupted teeth whether malposed or not may become very serious if not treated conservatively, as illustrated in my practice by the case of a young man who died of cavernous sinus thrombosis which had followed an attempt to remove a partly erupted malposed mandibular third molar during an acute infection of the surrounding soft tissues.

Infections of the bone are quite common in the mandible and maxilla on account of the frequency of dental caries. Conservative treatment of osteomyelitis is even more indicated in the jaws, as a loss of bone and deformities here cannot be taken care of as readily as in other parts of the body. Watchful waiting, evacuation of pus whenever or wherever it collects and removal of sequestra when fully developed will give the best results. A word of warning against curettage is essential because curettage is absolutely contra-indicated in osteomyelitis, acute or chronic, and is always the cause of extensive destruction of bone.

Of the diseases of the salivary glands, the formation of calculi is most frequent, although the calculus may be present for many years without symptoms. The sudden obstruction to the normal flow of saliva will cause excruciating pains and a marked swelling of the involved gland which only slowly subsides; such swellings will have a distinct outline corresponding to the position and form of the salivary gland. The vast majority of salivary calculi can be removed intraorally and without removal of the gland. The diagnosis can be confirmed and the operative procedure outlined by a proper x-ray examination.

The oral cavity is a very fertile field for the study of

tumors, not only microscopically, but especially from the clinical standpoint. Often tumefactions of the free gingiva are found, which microscopically show only chronic inflammation. Another group of tumor forms are the epulides which are somewhat on the borderline between true neoplasms and inflammatory conditions because they also show inflammation. As the name implies they are found upon the gum tissue or the ridge. Their successful removal necessitates the sacrifice of some of the surrounding healthy tissue including teeth, the amount of which can be determined by the experienced reader of the roentgenogram of the region. Related to this class of growths is the pregnancy tumor—termed angiogranuloma by Furedi, who made a valuable pathological study of the same—a tumor springing from the soft tissues of the mouth mainly the gingiva. Their surgical removal is indicated in all cases—although they disappear at times after pregnancy—to avoid their reappearance in later pregnancies and the loosening or loss of adjoining teeth. A study of the x-rays for the establishment of the correct diagnosis and outline of treatment is important. Of the true neoplasms there are found in the mouth most frequently the fibroma and osteofibroma, whose treatment coincides with that of the epulides. The care of a malignant tumor, like sarcoma and carcinoma, if circumscribed does not always require extensive resection, but complete removal which must include a safe margin of sound tissue and must be followed by radiation. Soon they will be more frequently detected in their very early stages, because education of the laity but particularly of the healing professions will be followed by early recognition and early treatment. The giant-cell tumor and osteitis fibrosa are proliferative masses rather than real neoplasms and will at times also have to be radiated. A great variety of tumors are found in the soft tissues of the hard and soft palate, all belonging to the group of mixed salivary tumors of benign and malignant variety, including adenocarcinoma and different gradations of basal-cell carcinoma. Local removal may not be sufficient and the study of many sec-

tions will determine the necessity for radiation. The most interesting tumors of the oral cavity are the ones originating from dental structures. The dental organ gives rise to simple, total and partial, and composite odontomas and cementomas; they are always benign. From the epithelium of the enamel organ originates the adamantinoma of the solid and cystic type. A preoperative biopsy may not be conclusive. A complete removal as of a malignant tumor is imperative, followed by a most thorough study of many sections, which so often reveal an atypical makeup or even a true carcinoma. Such cases naturally require radiation. It is best, however, to subject them all to this treatment. The subject of tumors cannot be dismissed without adding that the safest treatment for advanced (not circumscribed) malignant cases is in the hands of those surgeons and institutions who combine radium and x-ray treatment with their surgery.

In former years, trigeminal neuralgia was grouped amongst those conditions, the treatment of which was to say the least, ineffective. Since the perfection of the surgical operation for the relief of this complaint, namely, sub-total section of the sensory root of the fifth nerve by Frazier and Spiller, this malady can be entirely relieved. In the last 401 consecutive operations by Dr. Frazier the mortality has been two tenths of one per cent. Frazier says: "There is nothing obscure about trigeminal neuralgia save its origin." At times it may be difficult to differentiate trifacial neuralgia from atypical forms which are better termed facial pains. However, if one remembers that it attacks mostly patients past middle age and keeps in mind the unbearable typical paroxysmal pains, it seems that it can be differentiated from facial pains which are really entirely different, because not so severe, lasting for hours and relieved for a time by removal of teeth and different treatments, but always return. Although true major trifacial neuralgia is never relieved by peripheral operations or treatment of peripheral lesions, the patient should always be subjected to a thorough examination of the mouth, jaws and teeth and the mouth always put in

good condition, as it must also be done for those patients who suffer with facial pains, a relief for which is very rarely accomplished. Alcoholic injections are useful for diagnostic purposes and may be used as a method of treatment if the patient fully realizes that the injections are of only transitory effect. The neurologist and neurosurgeon should always be consulted in these cases, besides the family physician.

In conclusion I wish to say that the principle of periodic health examinations holds good for the mouth as well as any other part of the body. In fact, the dentists have appreciated this for more than fifteen years and have created the dental hygienist whose duty it is to subject a patient's teeth to prophylactic treatment and call the dentist's attention to the presence of any pathological condition. I go still further and believe that once a complete record of a patient's mouth has been taken by means of x-ray, pulp-test and transillumination—aside from the usual clinical records—the so-called bitewing x-ray examination which only shows the crowns and the neck of the teeth should be taken annually and only those teeth completely x-rayed which are devitalized. This x-ray examination in combination with the periodic treatment by the dental hygienist well trained in the recognition of the pathological conditions about the mouth will prevent many conditions, a successful treatment of which at the present time is either difficult or impossible.

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DEATHS OF FELLOWS OF THE ACADEMY

CARLOSS JAMES CHAMBERLIN, M.D., 114 East 54 Street, New York City; graduated in medicine from Vanderbilt University, Nashville, Tennessee, in 1922; elected a Fellow of the Academy January 3, 1929; died, July 16, 1931. Dr. Chamberlin was a Fellow of the American Medical Association, a Fellow of the American College of Surgeons, a member of the County and State Medical Societies, and Assistant Surgeon to Metropolitan and Skin and Cancer Hospitals.

HERMAN FERDINAND LAMPE, M.D., 34 East 51 Street, New York City; graduated in medicine from the Jefferson Medical College of Philadelphia, in 1915; elected a Fellow of the Academy November 1, 1923; died, July 20, 1931. Dr. Lampe was a Fellow of the American Medical Association, a member of the County and State Medical Societies, a member of the American Laryngological, Rhinological and Otological Societies, a member of Kings County Hospital Alumni Club, a member of the Alumni Association of New York Eye and Ear Infirmary, Aural Surgeon to the Midtown Hospital, Senior Assistant Aural Surgeon to the New York Eye and Ear Infirmary, and Otologist to the Broad Street Hospital.

JOHN OSBORN POLAK, M.D., 20 Livingston Street, Brooklyn, N. Y.; graduated in medicine from Long Island College Hospital, in 1891 and from the Medical Department of the University of Vermont, in 1891; elected a Fellow of the Academy June 6, 1895; died, June 29, 1931. At the time of his death, Dr. Polak was one of the Vice-Presidents of The New York Academy of Medicine. He was Professor of Obstetrics and Gynecology at the Long Island College Hospital Medical College, a Fellow of the American Medical Association and a member of many other medical societies. He was Instructor and Professor at New York Post-Graduate Medical School from 1894 to 1907. In 1903 he was Professor of Obstetrics and Clinical Professor of Gynecology at Dartmouth Medical School. Dr. Polak was the author of "Manual of Obstetrics" and "Manual of Gynecology" and of many papers and medical periodicals.

HENRY LYLE WINTER, M.D., 162 Grand Street, Newburgh, New York; graduated in medicine from New York University, New York City, in 1892; elected a Fellow of the Academy April 19, 1928; died, July 29, 1931. Dr. Winter was a Fellow of the American Medical Association, a Fellow of the American College of Physicians, a member of the County and State Medical Societies, a member of the American Society for the Advancement of Science and Neurologist to St. Luke's Hospital, Newburgh.